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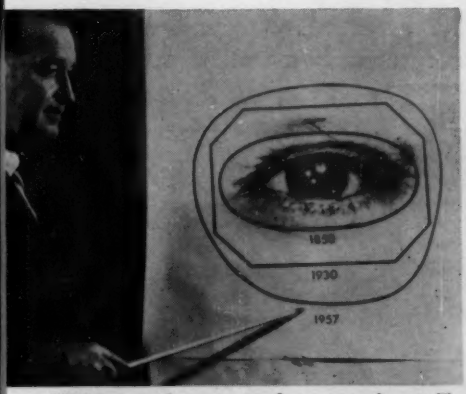

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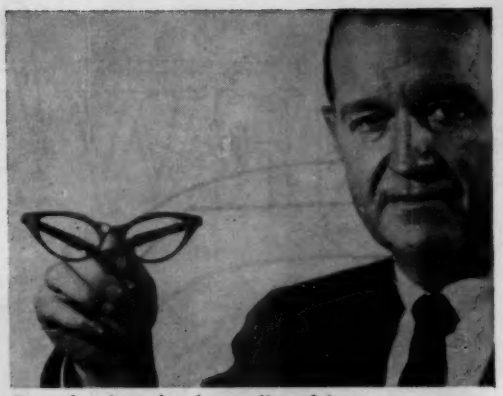

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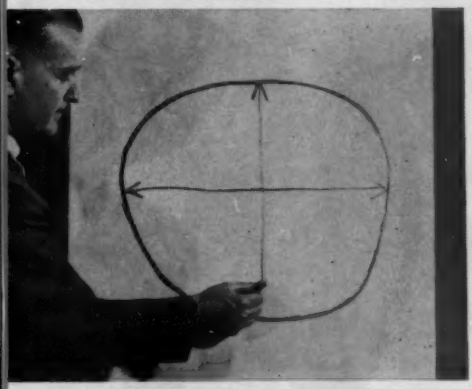

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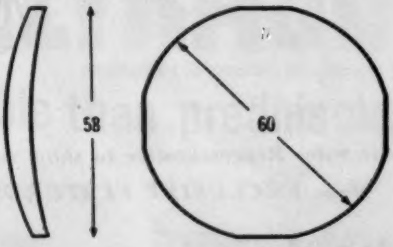

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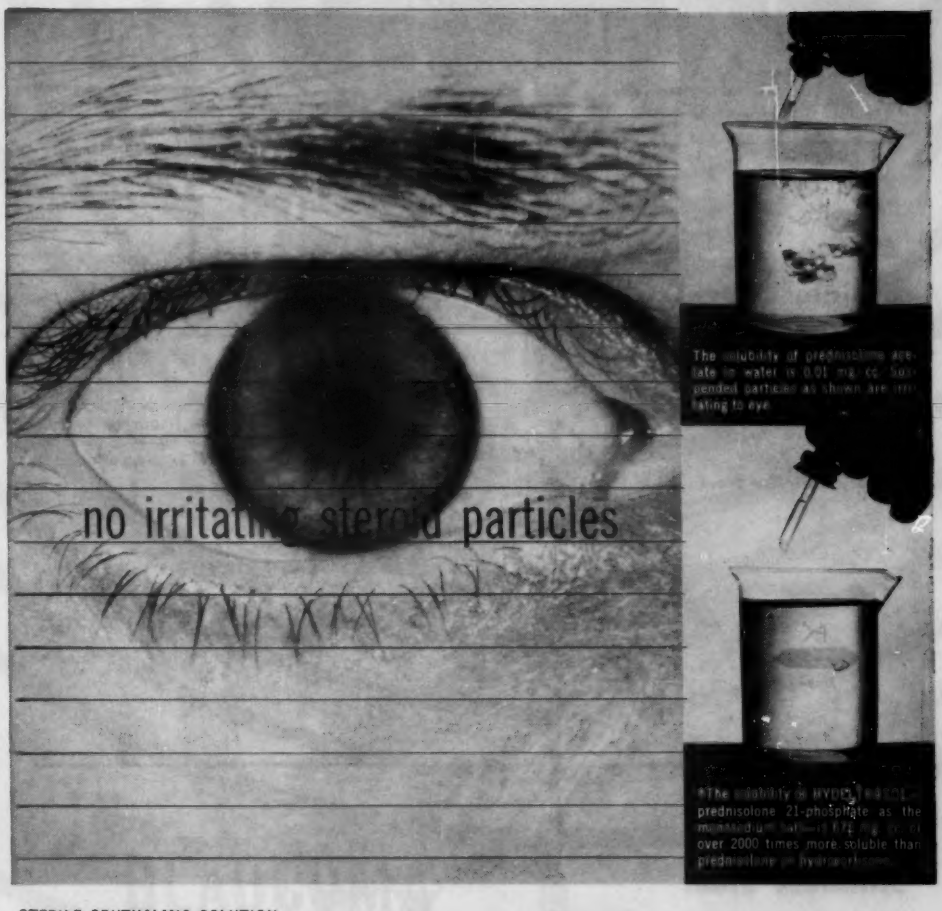
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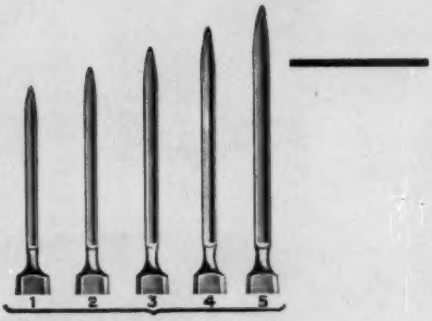

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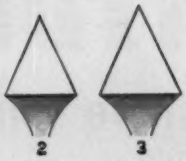

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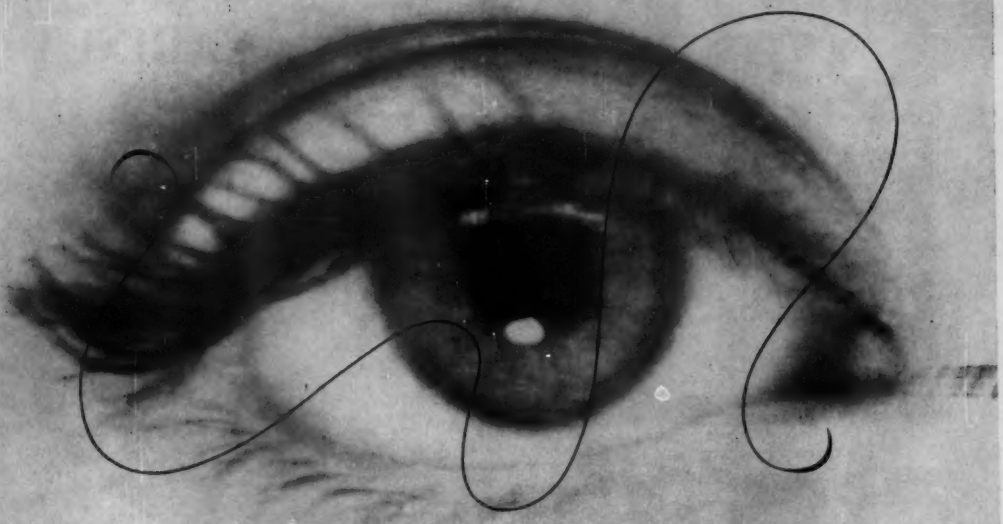

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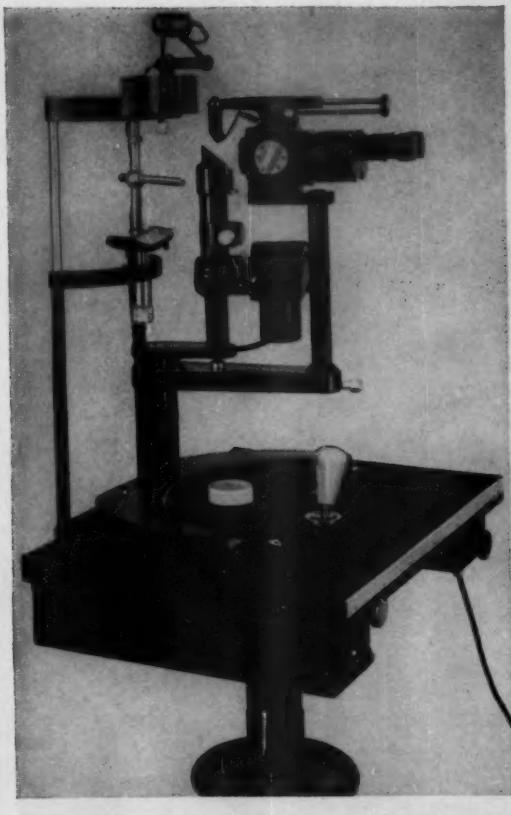

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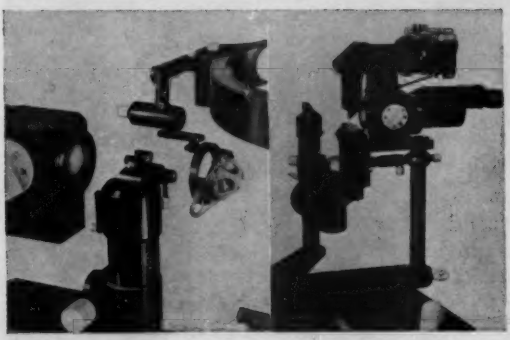

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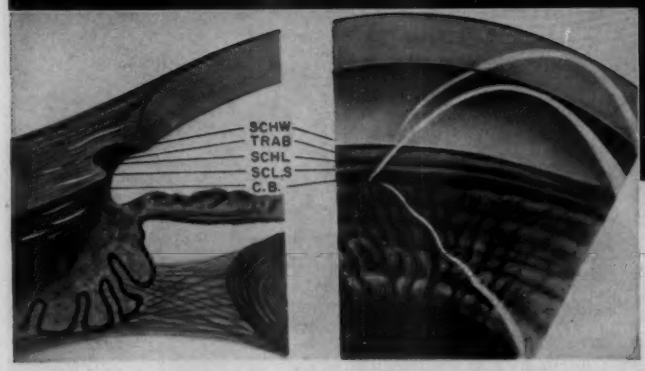

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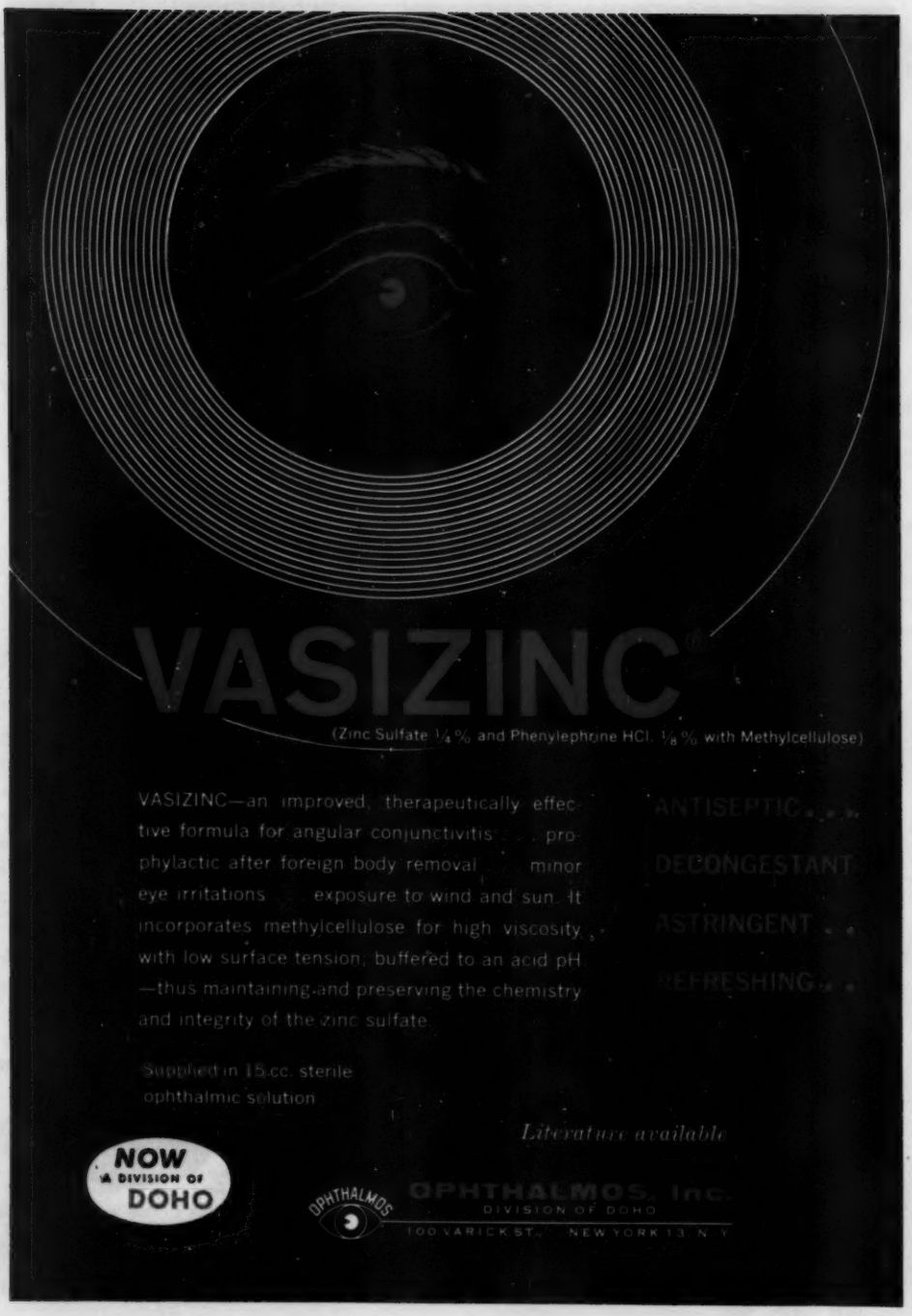
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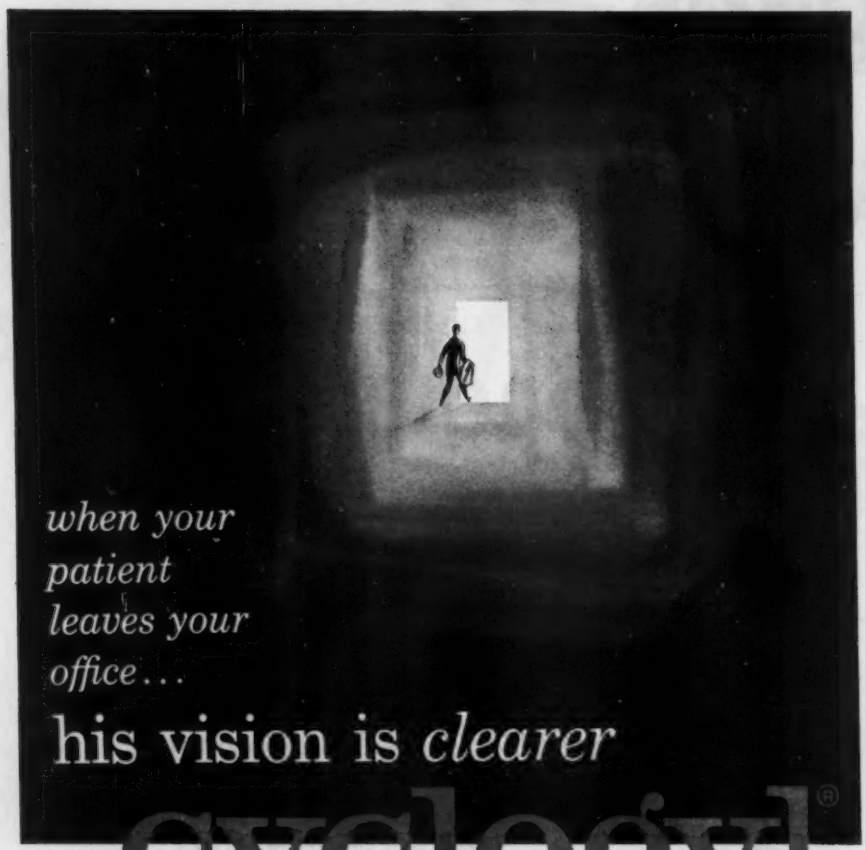

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Selection of Procedure for Cataract Extraction

WALTER S. ATKINSON, M.D., Watertown, N. Y.

The procedures to be discussed are for the extraction of senile cataracts.

A detailed history, thorough examination of the eyes, general physical examination, careful preoperative preparation, and good anesthesia and akinesia, so that the lids and eye are immobile with marked hypotony, will make any type of operative procedure for the removal of a cataract safer. With a soft eye the removal of cortical matter takes longer, but the hypotony makes both the extracapsular and intracapsular extractions safer and reduces the incidence of vitreous loss to practically zero. In order to be sure that the intraocular tension is low it is advisable to check the tension with a tonometer before making the section. Surgeons who insist upon these operative measures rarely have operative accidents.

In regard to the method of making the section, all ophthalmologists are familiar with the difficulties and hazards of a full Graefe section. These difficulties and hazards increase if preplaced sutures, particularly absorbable surgical (gut) sutures, and a limbus-based conjunctival flap are used.

To avoid these hazards, some surgeons make a small Graefe section and enlarge it with scissors. Other surgeons use a keratome or scleratome [1] to make the initial incision and enlarge it with scissors. With a keratome or scleratome it is easier and safer for the average surgeon to make the incision in the proper place.

A limbus-based conjunctival flap seems preferable to a fornix-based flap, chiefly because with the former an epithelial ingrowth would seem less likely to occur. The principal objection to the limbus-based flap is that it may be in the way and may make it more difficult to see the point of the knife in the anterior chamber. However, it can be held out of the way easily.

After the conjunctival flap is prepared, a section with long bevel made well forward in avascular cornea, just back of the attachment of the conjunctiva to the cornea, has several advantages. In this location it is easier to make the incision; the iris is less likely to be injured with the knife or scissors; there is less bleeding, and when the normal intraocular tension is restored the pressure against the inner beveled edge or shelf helps close the wound more securely. The incision may be beveled as much as is desired with a keratome or scleratome. The bevel can be continued with the scissors when the wound is enlarged, but it should be decreased as the 180-degree meridian is approached, so that the wound will open widely enough to allow easy extraction of the lens. Loss of the anterior chamber, with the well-known complications such as anterior synechia and secondary glaucoma, is less likely to occur postoperatively when a beveled incision is used. Neither this location for the section nor a long bevel is desirable when a basal iridectomy is to be done or if there is a large, flat, hypermature

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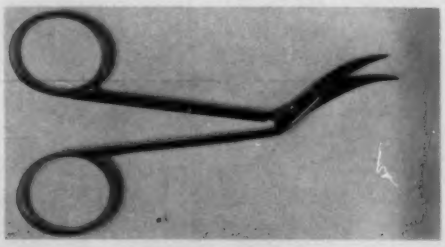
nucleus or if one wishes to grasp the capsule above at the equator. Under these circumstances a limbal incision is preferable.

If a keratome is used to make the section, a straight-sided keratome, such as the Grieshaber No. 13, the blade of which is 4 mm. wide and 11 mm. long, is preferred. Little pressure is required to introduce it, and light fixation is adequate. However, if an initial nonpenetrating incision or groove has first been made in order to introduce preplaced sutures, a broader keratome may be used because there is so little corneal tissue to penetrate and firm fixation is not necessary in order to hold the eye. The upper lip of the wound can be grasped for fixation or as light a fixation as the conjunctival flap may be used. If the conjunctival flap is used for fixation, its position can be readily changed so that the point of the keratome can be watched as it enters the anterior chamber. Practically no distortion of the globe occurs when the incision is made, and aqueous is rarely lost. Subluxation or dislocation of the lens with loss of vitreous, which occasionally happens when one is making a Graefe section, does not occur when the section is made with a keratome or scleratome, particularly if a nonpenetrating incision has first been made for preplaced sutures.

To enlarge the wound a modified Daviel scissors has proved most satisfactory, in my hands (Fig. 1). The scissors as Daviel described them [2] were "curved on the flat so as to follow the corneoscleral circle." The modified scissors have blunt points and a bend in the shaft, which makes them easier to use, and serrations on the blades similar to those on steak knives or barber scissors, so that they cut more easily and the serrations prevent them from slipping off or buckling the cornea.

Fig. 1.—Modified Daviel scissors; a bend in the shaft makes them easier to use and serrations on the blades make them cut more easily and prevent them from slipping off or buckling the cornea. (Made by V. Mueller & Co., Chicago, and Storz Instrument Co., St. Louis.)



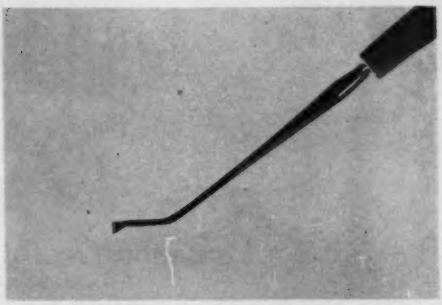


Fig. 2.—Scleratome—similar to a cystotome, but heavier. The blade is 0.75 to 1.00 mm. in length. The shaft is bent at an angle of 45 degrees at a distance of 3 to 5 mm. from the blade. (Made by E. B. Meyrowitz, Inc., New York, and Storz Instrument Co., St. Louis.) (Reproduced from Atkinson.[1])

Introducing any sharp-pointed knife, such as a Graefe knife or keratome, several millimeters into the anterior chamber to make the section is not without risk. To overcome this risk, the scleratome (Fig. 2) which is a different type of instrument, may be used. It looks like a cystotome, but it is heavier and has a blade 0.75 to 1.00 mm. in length. The shaft of the instrument is bent at an angle of 45 degrees at a distance of 5 mm. from the end of the shaft so that it can be held firmly against the globe to prevent the operator from making a perforating incision (Fig. 3,*A*, insert).

At first, as shown in Figure 2, the bend in the shaft was over 5 mm. from the blade. On the suggestion of Chandler,[3] the bend in the shaft has been made closer to the blade, which allows it to be held more firmly against the globe while the incision is being made. However, no harm is done if a perforating incision is made, and sometimes a perforating incision is desirable. It is as easy to introduce sutures after making a perforating incision in this manner as it is to do so after a keratome incision, but

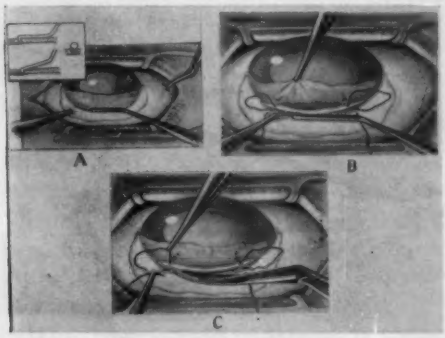


Fig. 3.—*A*, insert, shaft held firmly against globe to prevent perforating and tipped up to make a perforating incision. *A*, firm double fixation. The surgeon uses sharp-toothed forceps to obtain a firm bite of episcleral tissue near where the incision is to begin. The assistant grasps the tendon of the rectus muscle at its insertion on the opposite side of the globe with fixation forceps. The blade of the scleratome is introduced its full length, and the shaft is pressed firmly against the globe. The incision is made slowly to the desired length and depth in one stroke. *B*, two 000000 mild chromic gut sutures with large knots on the ends; upper lip of wound held by the surgeon and conjunctival flap by assistant to make perforating incision. *C*, suture held out of the way by assistant while the wound is enlarged with scissors. (Reproduced from Atkinson.[5])

sutures can be placed more accurately by the average surgeon before the chamber is opened. The importance of accurately placed sutures to close the wound firmly with the lips of the wound in exact apposition is well recognized.

In making the section with the scleratome,[4] a limbus-based conjunctival flap is first made in the usual manner. Firm double fixation is essential in order to make a long deep nonpenetrating incision with the desired bevel in one stroke with the scleratome (Fig. 3,*A*). The surgeon uses sharp-toothed forceps to obtain a firm bite of episcleral tissue near where the incision is to begin. The assistant grasps the tendon of the rectus muscle at its insertion on the opposite side of the eye with fixation forceps. To obtain a good clean deep incision with the instrument in one stroke, it should be very sharp, the blade should be introduced its full length, and the shaft, pressed firmly against the globe. The incision *should be made slowly*. Two 000000 mild chromic (Ethicon) gut sutures may then be introduced (Fig. 3,*B*). A perforating incision is then made, with the scleratome, through the bottom of the nonpenetrating incision and is enlarged with scissors (Fig. 3,*B* and *C*).

This method of making the section may seem unorthodox, but it is so much safer and easier than a Graefe knife or keratome that it merits consideration.

Prior to the time when the advantages of hypotony were appreciated, a Bard-Parker No. 15 blade was used to make the initial nonpenetrating incision for the introduction of sutures. However, when hyaluronidase is used in the anesthetic solution for the orbital injection and firm pressure applied over the eye for at least five minutes the hypotony produced makes it difficult to obtain a clean incision of the proper length and depth for preplaced sutures with a Bard-Parker knife. For this reason a different type of instrument, the scleratome, was devised. It is important to have the nonpenetrating incision long and deep, so that the wound will open widely enough to permit the sutures to be held or placed out of the way to avoid cutting them when the section is made.

Corneoscleral Sutures

Firm corneoscleral sutures decrease the danger of iris prolapse and allow the patient more freedom of movement following operation. The many types of sutures and their numerous modifications may be divided into two categories: preplaced sutures and postplaced sutures. The preplaced sutures have definite advantages. They are easier and safer to introduce, the interval between the time at which the section is made and completion of the extraction is shorter, and the pupil is less likely to contract. Of the preplaced sutures, one based on a modification of the principle suggested over 60 years ago by Surez de Mendoza[5] is excellent. Surez de Mendoza, it appears, was the first to advocate introducing sutures through the lips of a nonpenetrating incision before

the section is completed. When a beveled incision is used, two appositional sutures, one at about 11 o'clock and the other at 1 o'clock, are usually sufficient to hold the wound securely closed (Fig. 3,*B*). A large knot, double figure eight, at the end of the suture prevents it from being pulled through the cornea. The knot serves two purposes. In case of emergency, if it is desirable to close the wound quickly, this can be done by traction on the upper arm of the suture. The knot also makes it easier to hold the loop of the suture out of the way when enlarging the wound with scissors. This applies particularly to gut sutures, the loops of which tend to twist so that they lie across the partial penetrating incision. The gut sutures are also difficult to see and if not held out of the way may be cut. However, the advantage of not having to remove the sutures more than outweighs the disadvantages. Dunnington [6] has found that there is no evidence of stromal necrosis or of epithelial invasion with mildly chromicized surgical gut sutures. With nonabsorbable surgical (silk) sutures there is a rapid downgrowth of epithelium along the suture tract, which is another point in favor of gut sutures.

Postplaced sutures are more difficult to place accurately. However, even though preplaced sutures are preferred, there are occasions when one must be prepared to introduce sutures after the section has been made. A preplaced suture may be cut, or additional sutures may be considered advisable following the extraction.

Practice is particularly essential in order to facilitate the introduction of postplaced corneoscleral sutures accurately and to make it less hazardous. Fine sharp-toothed fixation forceps, such as the Elschnig or Castroviejo corneal forceps, to hold the lip of the wound, make introducing the sutures easier.

An often forgotten but well-known fact is that if the needle is grasped with the needle holder close to the point the needle will penetrate tough tissue more easily.

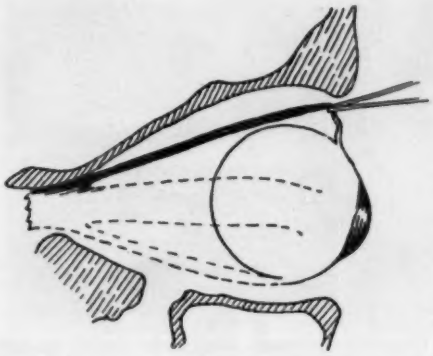


Fig. 4.—Suture under superior rectus, well back, to hold muscle away from the globe to avoid pressure on the eye.

A suture under the superior rectus muscle is no longer necessary to prevent the patient from looking up, since akinesia has been produced by an injection well back near the muscle. However, the eye can be moved to the desired position and the muscle held away from the globe to avoid pressure on the eye if a suture is placed well back under the superior rectus muscle (Fig. 4). This is an added protection against vitreous loss. Usually a retrobulbar injection followed by rotary massage and pressure produces akinesia of the other rectus msucles. If not, an injection of 0.5 to 1.0 cc. of the anesthetic solution about 3 cm. back near the muscle will produce akinesia, but occasionally there may still be some activity. This is more likely to occur if the preanesthetic preparation has not been adequate, in which event more sedative may be indicated and sutures similar to the superior rectus bridle sutures may be advisable. I am convinced that a little extra time spent before the operation to make sure that the lids and eye will be quiet, with no pressure from either the lids or rectus muscles, is good insurance against vitreous loss. A canthotomy should be done if the lids are tight and cause pressure on the eye. If a hemostat is placed tightly at the site to be incised before cutting with the scissors, annoying bleeding may be prevented.

Regardless of the instruments used to make the section, the position of the section and the amount of bevel are influenced by the type of cataract.

If the cataract is immature or mature, the section may be either limbal or corneal and with a long bevel.

If the cataract is hypermature, with a large flat nucleus, a limbal incision with a short bevel is indicated and a complete iridectomy is often advisable.

If a corneoscleral trephining or other filtering operation has previously been done and there is a good filtering bleb, four locations for the section have been advocated:

1. In the usual position at or near the limbus, disregarding the bleb. When the section is made in this position, the bleb is generally destroyed.

2. In the cornea just below the bleb. When made here, the wound does not heal as readily; more sutures are advisable to prevent losing the anterior chamber postoperatively and the ingrowth of epithelium. If the conjunctiva is dissected up to form a fornix-based flap, filtration will probably be stopped when the wound heals.

3. Temporally. In this position, the filtering cicatrix can be avoided. It may be necessary to do an iridectomy nasally or an iridectomy temporally if the pupil is small.

4. Below. In this position, the procedure is a bit awkward. Here also an iridectomy or iridotomy may be advisable. In all positions it may be necessary to free posterior synechia.

When the cataractous lens is subluxated or dislocated and is in the anterior chamber, an ab externo incision is desirable, and for this type of incision the scleratome is excellent. Preplaced sutures arranged so that they can be pulled up easily and quickly to close the wound are helpful.

For the hypermature Morgagnian cataract with secondary glaucoma, the tension can usually be lowered with miotics, acetazolamide (Diamox), or retrobulbar injections. If not, the eye should be decompressed slowly, allowing about 20 minutes for the procedure. One can then proceed with the usual section. Before removing the cataract it is advisable to irrigate the anterior chamber to remove toxic products which are said to be produced by the hypermature cataract and to permeate the lens capsule. If the pupil is small owing to use of miotics, an iridectomy may be necessary. An intracapsular extraction with the erisophake is the operation of choice.

When corneal dystrophy complicates the cataract, McLean[7] recommends a scleral section with complete iridectomy and a top-first, sliding delivery of the lens. There is considerable bleeding, which is disturbing, but the cornea is not affected as much as with the usual section.

When there has been an old iridocyclitis with atrophic iris, and the pupil is secluded or occluded, one operation, intracapsular extraction, usually with iridectomy, is generally conceded to be the operation of choice. In the past, preliminary iridectomy followed later by extracapsular extraction has been advocated and we have been cautioned to remove the anterior capsule by twisting to tear it with toothed forceps in order to avoid traction on the ciliary processes. In this type of case the zonule is usually exceedingly friable, and, when the anterior capsule is grasped with toothed forceps, the lens often dislocates and can easily be removed in capsule. It, therefore, seems advisable to use smooth capsule forceps or an erisophake and remove the cataract in capsule.

Occasionally, when the iris is pulled up for iridectomy, the posterior synechia are broken. In some cases the pupil is firmly adherent to the anterior capsule and to the thick organized exudate in the pupillary area. If it is not freed when the iridectomy is done, a spatula can be introduced and the iris and exudate can be separated from the capsule. The blunt blade of deWecker scissors can then be introduced and carried well below the pupillary area so that the incision includes the exudate which occludes

the pupil and extends well into the iris below. Usually the iris springs apart, making a good pupil. If not, it may be advisable to remove a wedge of the exudate and iris. The lens can then be removed top first with comparatively little trauma.

Intracapsular Extraction

A few steps in the technique of intracapsular extraction should be emphasized. The importance of a large section and of slow dislocation and delivery of the lens has been stressed by Knapp.[8] Elschnig's[9] method of making an iridotomy with the deWecker scissors without grasping the iris with forceps seems worthy of emphasis. To do this, the corneal flap is raised, and the iris is then picked up on the point of one blade of the scissors and snipped. This can be done safely and easily if both blades of the deWecker scissors are blunt and of the same length. The objection has been made that the lens capsule may be nicked with the scissors, but this does not occur if the points of the scissors are blunt and directed upward and toward the limbus, where the lens is further from the iris. One iridotomy at 12 o'clock may be sufficient, but, since prolapse may also occur on either side, an iridotomy at 10 and another at 2 o'clock make such an occurrence less likely. However, with the wound securely closed with corneoscleral sutures, severe trauma is usually necessary to cause a prolapse, and in such an instance neither iridotomies nor sutures will prevent it. The two additional iridotomies are also a protection against pupil block.

For years the capsule forceps have been the most popular instrument to aid in the dislocation and delivery of the lens in capsule. The Castroviejo cross action capsule forceps, a modification of the Arruga forceps, ruptures fewer capsules than others that I have used. Careful inspection of the forceps should always be made before they are introduced to make certain that the blades come together accurately[10] (Fig. 5), that they are smooth, and that there are no cotton strands or other foreign particles on them.

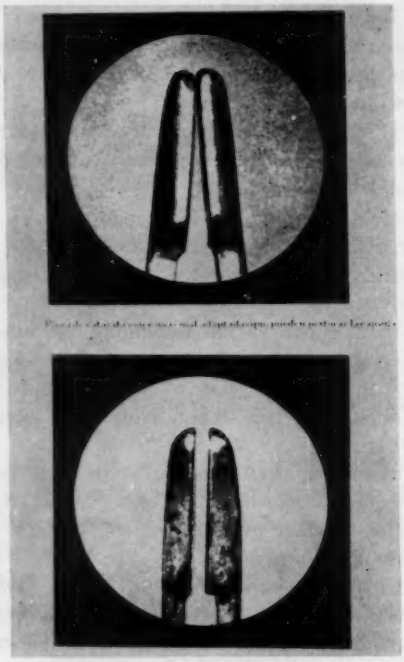


Fig. 5.—Capsule forceps. Blades of capsule forceps on the left show good adaptation of the tips, and those on the right, poor adaptation of the tips. (Reproduced with permission from Arruga,[10] The Blakiston Company [Division of McGraw-Hill Book Company, Inc.].)

The following points in regard to tumbling the lens cannot be overemphasized. The capsule should be grasped well down toward the equator, back of the iris, if the pupil is not widely dilated. Traction to dislocate the lens below should be made by lateral movements of the forceps from side to side and then down and a little forward toward the cornea while pressure is exerted with the hook or whatever instrument is preferred for the purpose. Often the tendency is to pull up with the forceps, which pulls the upper edge of the lens up back of the iris and makes tumbling more difficult. The proper regulation of the amount of traction and pressure as the lens begins to tumble or deliver and the folding of the cornea back of the lens with the hook should be particularly stressed. Folding the cornea back

of the lens is a most important maneuver, which holds the vitreous back and aids in the delivery of the lens, particularly when the eye is soft. It also allows the hyaloid and vitreous to be cleared from the posterior capsule when it is adherent.

With marked hypotony, the mechanics of the intracapsular extraction are changed. Practically no vitreous pressure is used. The surface of the vitreous can often be seen back of the iris plane; it appears flat and apparently does not assist in the delivery of the lens. It is said that, with marked hypotony, it is difficult to grasp the capsule and that the lens may be pushed back into the vitreous. Such an occurrence can be avoided by exerting pressure on the sclera with a hook posterior to the lens in the 6 o'clock meridian to hold the lens forward while the capsule is being grasped.

The erisophake has become increasingly popular, particularly for the extraction of intumescent and Morgagnian cataracts. Many surgeons use it routinely instead of capsule forceps. An important point in the use of the erisophake is occasionally forgotten; if it is placed on the center of the lens with the shaft of the instrument at an angle of not more than 15 degrees from the horizontal meridian, it is easier to rotate the erisophake and tumble the lens within the eye. A soft eye adds to the ease and safety of this maneuver. Practice to attain skill in using this instrument amply repays the surgeon.

The tendency now is to select the method or combination of methods of extraction best suited for each patient, and the surgeon who has mastered the various methods will have a high percentage of good results.

A careful analysis and comparison of the results of one's cataract surgery with those of others allows one to evaluate his surgery and calls attention to faults which, if corrected, will lead to better surgery.

129 Clinton St.

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Atypical Retinitis Pigmentosa, Acanthrocytosis, and Heredodegenerative Neuromuscular Disease

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The paper of Kornzweig and Bassen published in the A. M. A. ARCHIVES OF OPHTHALMOLOGY in August, 1957, "Retinitis Pigmentosa, Acanthrocytosis, and Heredodegenerative Neuromuscular Diseases," is of current interest. This intriguing combination of abnormalities has been reported to date in only three patients, the two pationts of Kornzweig and Bassen and the one of Singer, Fisher, and Perlstein. The patient of Singer et al., as known to Kornzweig and Bassen, exhibited the entire complex except for the retinitis pigmentosa. This patient, the son of first cousins, developed celiac disease at about the age of one year which was controlled by low-fat diet. At the age of 9 years acanthrocystosis was discovered, and at the age of 10 the insidious onset and slow progression of ataxia, intention tremor, athetoid movements, and impaired proprioceptive sense was noted.

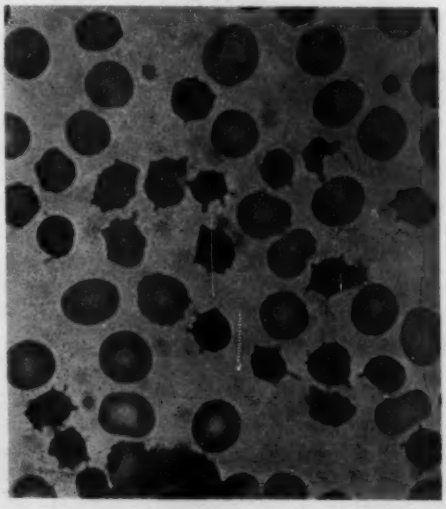
It is the purpose of this paper to report a follow-up examination of the patient of Singer et al. performed in December, 1956, about six years after their original investigation. We think we can supplement the paper of Kornzweig and Bassen and provide some additional information of great interest.

Report of the Case

In the interim years the patient showed continued progression of ataxia, intention tremor, and involuntary movements. He became incapable of caring for himself. Over a period of about three years he became aware of a gradual deterioration in his vision. Also, a definite intellectual decline was noted by his parent.

Neurological Examination.—The patient was a chronically ill 19-year-old white youth. He was unable to speak and would respond to questions by nodding. His head was tonically turned to the right. Periodic involuntary bobbing dystonic movements of his head were noted to be exacerbated when the patient was subjected to stress. The upper extremities exhibited similar involuntary movements with an athetoid quality. There was marked cerebellar ataxia, involving all four extremities. Volitional movements of the lower extremities was so uncoordinated that the patient could neither stand nor walk. The muscle tone was generally decreased, and the deep tendon re-

Fig. 1.—High-power view of blood film of patient of Singer et al., showing acanthrocytes with their characteristic thorn-like unevenly spaced processes of varying length and width.



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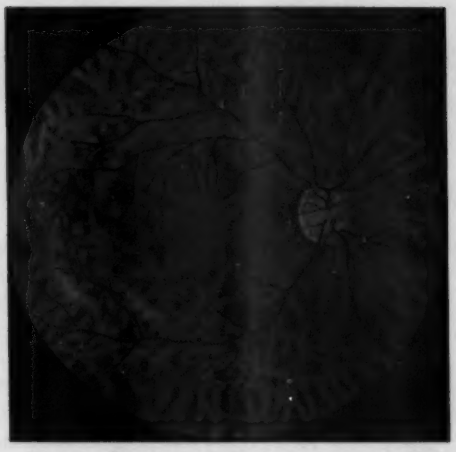

Fig. 2.—Drawing of fundus of same patient. Fundus photography was precluded by nystagmus. The artist has attempted to illustrate the following characteristics: a waxy-appearing disc, attenuation of the venules and arterioles, disorganization of the deep pigment in the midperiphery overlaid by glistening highlights, and a distinct gliosis of the macula.

flexes were suppressed. Motion, position, and vibratory sense could not be elicited up to the level of the clavicles.

General Physical Examination.—Except for gonadal atrophy there were no remarkable findings.

Ophthalmic Examination.—The maximum visual acuity obtained with correction was 20/400 in both eyes. The patient could not read the largest Jaeger type. The pupillary reflexes were normal. There was dissociated nystagmus on right and left lateral gaze. The point of basal convergence was poor. Ophthalmoscopic examination revealed clear media bilaterally. The optic papillae were sharply outlined and normal in size and shape, but they had a definite waxy yellowish pallor. They contained physiological depressions but no visible lamina cribrosa. There was bilateral peripapillary chorioretinal atrophy. The retinal arterioles and venules showed a marked diffuse attenuation. The retinal peripheries were highly tessellated. In the intermediate retinal areas there were many glistening highlights having a distinct gelatinous shagreen, and the deep pigment in this area was characterized by disorganization and definite clumping. However, there was no typical bone corpuscular pigment configuration. In the macular areas of the retinas the foveal reflex was not visible and there was a distinct gliosis of the internal limiting membrane. Biomicroscopy revealed no abnormalities in either eye. The visual fields were irregularly contracted to approximately 20 degrees with a 3/330 white test object. No annular scotomas could be demonstrated.

Laboratory Findings.—Blood: Hemoglobin, 3.8 gm., or 85%. Red cells, 5,000,000; "thorn-like" cells with irregular projections were present in large numbers, acanthrocytes. Hematocrit value, 45%; mean corpuscular volume, 90 cu. μ. White cells, 5900, with 41% polymorphonuclear cells, 7% band cells, 34% segmented cells, 30% large lymphocytes; 24% small lymphocytes, 4% monocytes, 1% eosinophils; platelets, normal.

Urine and Stool: Normal except for high stool fat content.

Chemistry Studies: Fasting blood sugar, 74 mg. per 100 cc.; nonprotein nitrogen, 30 mg. per 100 cc.; total cholesterol, 37 mg. per 100 cc.; cholesterol esters, 23 mg. per 100 cc.; free cholesterol, 14 mg. per 100 cc.

Free-Flowing Electrophoresis: Analysis of the serum protein by free-moving boundary electrophoresis by the Tiselius technique revealed the following findings: The albumin and α_1- and α_2-globulins were normal. There was a low γ-globulin and a low β-globulin value. The decrease in the β-globulin fraction is an interesting observation in view of the fact that in this patient a low total cholesterol value was secured. In general, this fraction of serum globulin reflects cholesterol levels of the serum.

X-rays: Head and chest revealed no abnormalities.

Conclusion

With the passage of years the patient of Singer et al. has developed retinitis pigmentosa and now has the complete syndrome. A

new feature is his phenomenally low serum cholesterol value, one of the lowest recorded at the University Hospital. The low cholesterol level was repeatedly confirmed by our endocrinologists. It would be interesting to know the serum cholesterol levels in the patients of Kornzweig and Bassen.

It is probable that the entire syndrome is basically an inborn error of fat metabolism producing a harmful effect on erythrocytes and nerve cells. It is suggested the careful blood studies are indicated in all unusual cases of retinitis pigmentosa.

University Hospital.

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Radioactive Isotopes

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The great scientific advance of our time was the splitting of the atom and all that accompanies it. The influence of radioisotopes on medicine is so great that any modern physician must have a basic knowledge of radioisotopes and their uses. The modern ophthalmologist is no exception. It is the purpose of this paper to acquaint the ophthalmologist who knows little or nothing of radiobiology with the basic and important concepts in this field as related to ophthalmology.

It will be necessary to present first a few fundamentals in the understanding of radioisotopes. Following this the use of radioisotopes in diagnosis in therapy and in research in ophthalmology will be discussed.

The problem of understanding the important basic principles of radioisotopes as applied to ophthalmology can be made very simple. Many of the terms used in radiobiology, such as neutrinos, positrons, etc., need be of no concern to us. Although there are more than 1200 isotopes, each with characteristic half-lives, emissions, and energies, only a few need be discussed here.

Basic Concepts

An atom consists of an inner section, or nucleus, around which rotate small particles called electrons, which have one negative charge. The nucleus of most atoms is composed of both protons and neutrons. The protons have a mass 1840 times that of the electron and have one positive charge. The neutrons have the same mass as the protons but contain no charge. The chemical behavior of an element is determined by the number of protons in the nucleus and hence the number of electrons normally in its outer shells. If two substances contain the same number of protons and electrons, but a different number of neutrons, they will be chemically identical, although they have different atomic weights. Because they are chemically identical they occupy the same place in the periodic table and hence are called isotopes (from the Greek *isos* and *topos*, meaning the same place).[1] Many isotopes give off emissions from the nucleus which cause them to be radioactive. Only the three naturally occurring forms of radioactive emissions need concern us: These are α-, β-, and γ-emissions.

Alpha-particles are composed of two protons and two neutrons. They are helium atoms without the two electrons that normally exist in the outer shell and therefore possess two positive charges and have a mass of 4. Because of their great mass and strong charge they will not penetrate through unbroken skin. When an α-particle travels through tissue it strongly attracts electrons from the atoms of the tissue. The α-particle is going too fast to take them along, but the atom is left in an ionized state. An α-particle with 1 mev of energy will only travel through approximately 7.5μ of tissue, but in this short distance it creates many ions and hence is very damaging to the tissue.

Because of their poor penetrating power and great toxicity, α-particles are of little use in ophthalmology. Shaeffer[2] injected

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From the Department of Surgery, Division of Ophthalmology, Stanford University Medical School.

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astatine (At^{211}), a pure α-emitter, into a cyst in the anterior chamber, hoping to cure it by the heavy localized radiation of the α-particles. The idea was excellent, but the cyst was not cured.

Gamma-emissions are the equivalent of x-rays. They have no charge, little mass, and are the most penetrating and least toxic of the three emissions.[3] Ninety-nine per cent of γ-emissions of 1 mev are stopped in 70 cm. of tissue. Because these emissions penetrate through the entire head, they are of little use in ophthalmology. If an isotope emitting γ-radiation is given intravenously and a Geiger-Müller tube is held over the eye, the radioactivity from the entire head "drowns out" the radioactivity from the eye itself (Fig. 1).

Beta-particles are therefore the only emissions that are ordinarily useful in ophthalmology. They are electrons, the same as those in a wire carrying an electric current, but with more energy. They have one negative charge. Their penetrating power varies with the isotope from which they are derived. For example, the β-rays emitted by radioactive phosphorus (P^{32}) penetrate through a maximum of 8 mm. of tissue, with an average penetration of 3 mm. of tissue. This is a relatively high-energy β-particle. The β-emissions of S^{35} and a number of other isotopes do not have sufficient energy to penetrate through the sclera.

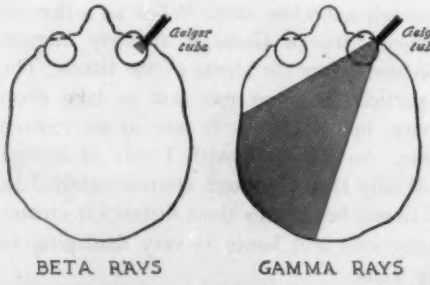

Fig. 1.—Gamma-rays from much of the head enter the Geiger tube and "drown out" any signal from the eye itself. The β-particles penetrate such a short distance that only those from the eye enter the Geiger tube.

Inspection of a chart of radioisotopes discloses that they number well over a thousand, but if we limit our choice to those isotopes which emit only β-particles and further restrict it to those isotopes from which the β-emissions have sufficient energy to penetrate through the sclera the list is shortened to a precious few.

There are other essential qualifications for a radioisotope if it is to be useful for our purposes. The half-life, the uptake or distribution in tissues, and the toxicity of its compounds must also be considered.

When a radioactive isotope gives off its emission, it becomes inert, or decays. A radioactive isotope decays at a rate specific for that particular isotope. The time required for 50% of a radioisotope to decay is called the half-life. For ophthalmic use the half-life must be long enough to be practical and not so long as to be dangerous. For example, O^{15} has a half-life of only 2.1 minutes, which causes it to be useless for clinical purposes because it would have largely decayed by the time it was taken from the cyclotron to the patient. Sr^{90} has a half-life of 25 years, which is too long to permit safe use around a laboratory. A rabbit given an injection of this material would have to be buried at sea; if Sr^{90} were spilled in the laboratory, the room might have to be closed for 150 years. A useful, less dangerous half-life is of the order of several days to a few weeks.

The physical decay of an isotope goes on whether it is in a test tube or in an organism. In the living organism the isotope is eliminated as are most chemicals. Therefore, the biological half-life is determined by the rate of decay of the isotope plus the amount eliminated from the organ or organism.

The uptake of various elements by different tissues must also be considered. Fe^{59} goes selectively to red blood cells, Zn^{65} to white blood cells, colloidal Au^{198} to lymphatics, and I^{131} to thyroid tissue.

The widespread use of P^{32} in ophthalmology has been due to the exacting re-

quirements of type of emission, physical and biological half-lives, uptake, and distribution, as discussed. P^{32} is a pure β-emitter. The β-ray has an energy of 1.7 mev, which is sufficient energy to penetrate through an average of 3 mm. of tissue, a maximum of 8 mm. It decays with a physical half-life of 14 days, but in the human organism elimination from the body reduces the remaining radioactivity to 18.5% of the original dose at 14 days. The distribution of phosphorus is ubiquitous, but it tends to concentrate in bone marrow and in nucleoproteins. All these facts make P^{32} nearly ideal for certain types of diagnostic and experimental work in ophthalmology.

Radioisotopes in Diagnosis

Radioisotopes are of occasional use in diagnosis and in therapy and of considerable use in investigative work. We shall consider first their use in diagnosis.

P^{32} has been widely used in the differential diagnosis of malignant melanomas from other lesions simulating these tumors. P^{32} was first used in the differential diagnosis of skin tumors in 1942, but a biopsy of surface tumor is easier and more accurate. For tumors in the eye, removal of tissue for biopsy may be impossible or dangerous and aspiration biopsies may be unreliable as well as dangerous.[8] For this reason, the P^{32} test for malignancy has become popular.

The technique for the use of P^{32} in the diagnosis of intraocular tumors is as follows.[9]

P^{32} in the form of buffered sodium phosphate, in which the phosphorus of the phosphate is the radioactive P^{32}, is given intravenously. The usual dose in adults is 500μc., which is the same as 0.5 mc. This dose is larger than a tracer dose, but it cannot be reduced much below 500μc., or a statistically significant number of counts cannot be obtained in a reasonable length of time. One must be able to obtain more than a hundred counts in a minute or less, because neither the patient nor the examiner can hold still for long periods. The dosage cannot be very much greater than this (750μc. is sometimes used [10]), because much larger doses depress the bone marrow.

During the first few minutes after injection, the P^{32} is distributed throughout the blood stream. It then diffuses into the tissue and enters into various combinations with the proteins, fats, and carbohydrates. Soon after injection the P^{32} is largely concentrated in or near blood vessels, and hence counts of radioactivity at this time are an indication of vascularity of the tissue. P^{32} is taken up by melanomas to a greater degree than by normal ocular tissues, and it is retained in the melanoma tissue for a longer time than in normal tissues.

If a Geiger-Müller tube is placed over a lesion and the counts obtained are compared with counts obtained over comparable areas elsewhere in the eyes, a higher counting rate suggests a more metabolically active tissue and hence a malignant tissue. However, a count obtained soon after the injection may be higher simply because the tissue is more vascular. For this reason, many authors have suggested that later counts would be more reliable. Terner, Leopold, and Eisenberg [11] advocated that a count be taken 1 hour after injection and 24 hours later. They felt that the initial (1-hour) count should be 30% higher than comparable areas in the same eye or the other eye and that the count 24 hours later should be proportionately still higher.

The use of P^{32} for the diagnosis of intraocular melanomas met with some enthusiasm and rather widespread use. It soon became apparent, however, that the method had definite limitations and that, although it was helpful, it was not a substitute for good diagnostic acumen. It is of interest that in most series the incidence of fallacious diagnosis is 10%, in spite of the elimination of obvious sources of error. In most series in which the diagnosis is based on clinical judgment alone the incidence of fallacious diagnosis is approximately 10%.[12] It would seem, therefore, that the use of P^{32} in the

diagnosis of intraocular melanomas might be useful as a laboratory adjunct in diagnosis, but it is certainly not a substitute for clinical judgment.

The defects of the P^{32} test may be summarized as follows.

1. Mechanical limitations. (*a*) It was previously mentioned that the β-emissions of P^{32} travel a maximum of 8 mm. through tissue and that the average only penetrate 3 mm. Most melanomas or lesions confused with them are in the posterior portion of the globe, and the emissions from this area will not reach a Geiger-Müller tube placed anteriorly. Therefore, an incision must be made in the conjunctiva and a curved tube placed behind the globe.[13] The curved type of Geiger tube is much less efficient than the straight one, and other types of probes [14] impose other difficulties. (*b*) If the counting probe is over thicker tissue that is active metabolically, such as rectus muscle or ciliary body, a false high count may be obtained.[15] (*c*) If the counting probe is tilted so that β-particles gain access to it from extrabulbar tissues, a false high count will be obtained.

2. Other lesions than tumors, specifically inflammatory lesions and areas of previous diathermy coagulation for retinal detachment, will result in a high count. Fortunately, most inflammatory lesions are recognized as such clinically and are not referred for P^{32} tests.

3. The specific uptake of P^{32} by melanomas is not great (10 to 13 times that of adjacent ocular tissue). The uptake ratio with I^{131} in thyroid malignancy is 1000 to 10,000 times that of other tissue. The difficulties associated with this relatively low uptake are compounded by adsorbtion of some of the β-emissions by the overlying sclera and by emissions from the conjunctiva and rectus muscles.[17]

Iris lesions, because of their accessibility would seem to offer ideal conditions for the P^{32} test. The results are not completely reliable, however, possibly because of the relative low metabolism associated with the low malignancy of these lesions.[18,19]

Retinoblastomas have been extremely misleading in their response to P^{32}. In addition, pediatricians do not look with favor on small children getting P^{32} when their bone marrow and other bone-forming organs are developing.[10]

Other radioisotopes, notably I^{131} in the form of diiodofluorescein, have been evaluated as aids in uptake studies but have been less rewarding [20,21] than P^{32}.

Summary.—It is my opinion that P^{32} may occasionally be useful in the clinical differential diagnosis of intraocular melanomas. The results are not so certain that they can be relied upon to the exclusion of clinical judgement. If my judgement differs from the results of the P^{32} test, I always rely upon the former and believe that others should do likewise. I no longer use the test for retinoblastomas.

Use of Radioisotopes in Therapy

The only very successful uses of isotopes in therapy are those concerned with external application to the eyeball. The most important of these are the Sr^{90} applicator for external therapy and the use of radon seeds applied to the sclera for the treatment of retinoblastomas. Many other ingenious and dramatic uses of radioisotopes in therapy have been tried, but they are mainly of academic interest.

The widely used Sr^{90} applicator was introduced into ophthalmology by Friedell, Thomas, and Krohmer.[22] Sr^{90} has certain excellent characteristics for this purpose: Its half-life is 25 years, which permits an applicator to be used a long while without recalibration; it is a pure β-emitter of good energy, and so it penetrates superficial tissue without going too deep, and the absence of γ-emissions decreases the hazard to the operator and to the patient as well; its chemical characteristics make for ease of handling; it is available and relatively inexpensive.

Sr^{90} decays to Y^{90}, with the emission of weak β-rays which have a peak energy of 0.65 mev and a half-life of 25 years. Y^{90}

then decays to stable Zr^{90}, emitting a strong β-radiation with peak energy of 2.16 mev and a half-life of 62 hours. It is the last emission which is the effective one. The important characteristic is that the half-value layer is approximately 1 mm. of tissue: That is, the dose 1 mm. from the surface is 50% of the surface dose; that 2 mm. from the surface is 25%; 3 mm. is 12.5%, etc.[23]

The Sr^{90} applicator soon largely replaced the older radon applicator,[24,25] radon being less readily obtainable, more expensive, and giving rise to a small but definite γ-emission.

When β-ray therapy was first introduced, it was used in the treatment of a remarkable number of ocular disorders: vernal conjunctivitis, tuberculosis of the anterior segment, superficial and deep keratitis of diverse etiology, corneal nebulas, maculas, etc.

An acute realization of the need for caution and the possible late effects of any radiation soon made itself known. Not only cataracts[26] but also a number of other later complications of β-ray therapy were noted. Merriam[27] presented late complications of β-ray therapy which might be summarized as follows.

Telangiectasis of the conjunctiva with doses of 3000 to 5000 rep, appearing approximately five years after therapy and being mainly a cosmetic blemish.

Superficial punctate keratitis, which is transient and lasts from four to six weeks with doses up to 5000 rep. It may last for months with higher doses.

Keratinization of the conjunctival epithelium with doses of 5000 to 10,000 rep; this persists for life and may be more annoying than the original lesion for which therapy was administered.

Radiation cataract; this has occurred with surface doses of 2300 to 22,000 rep.

Corneal vascularization and scarring, iritis and iris atrophy, and scleral atrophy have been noted with very high doses: 20,000 to 30,000 rep.

As more time has elapsed, the indications for β-ray therapy have become more sharply limited, the doses have become more restricted, and the complications have been greatly reduced.

Dr. Stevenson, in charge of β-ray therapy at Stanford Medical School, is now limiting dosage to 5000 to 6000 rep. The highest dose he has given is 16,000 rep. With this dosage schedule he has only observed two types of complications.

1. Punctate staining and irritation without punctate staining. This complication has occurred routinely with doses greater than 10,000 rep and occasionally with smaller doses. It has been helped but not cured by steroid ointments, has a duration of two weeks to six months, and has not proved incapacitating.

2. Telangiectasis. This complication seems to be unrelated to the dose. It occurs in those patients who were treated late, after a recurrent peterygium; that is, the capillary loops had already grown over the limbus. It is a real cosmetic problem.

It has been my feeling that the only common indication for β-ray therapy is recurrent pterygium and occasional wildly growing primary pterygiums. Beta-ray therapy is rarely indicated for keratoplasty, since steroids are more effective; vernal catarrh is helped somewhat but not dramatically; lid carcinomas are better treated with γ-rays or x-rays to ensure adequate penetration.

The therapy of intraocular tumors, usually retinoblastomas, by suturing radioisotopes to the sclera,[29,31,34] imbedding them in the tumor,[31] or distributing them on dental stents which are sutured to the sclera is not new. Radon seeds have been most commonly used. They depend upon β-emissions for their therapeutic effect, the α-emissions not penetrating the eye and the γ-emissions being very weak. More recently, radioactive tantalum wire (Ta^{182}) has been sutured to the sclera for treatment of retinoblastoma.[35] Ta^{182} emits both β- and γ-rays. It has also been used in the treatment of a rapidly growing, inoperable, melanoma of the iris.[36] It is my opinion that the radiation

therapy of retinoblastomas is better administered by the linear accelerator (6 mev x-ray) * or by the technique of Reese and his co-workers[37,38] than by use of radioisotopes. An isotope which depends upon β-emissions for its therapeutic effect may not penetrate effectively into cells of the tumor or to other seedlings of the tumor. An isotope which depends on the more-penetrating γ-emissions may cause uncontrollable damage to the remainder of the eye. Malignant melanomas in the one-eyed patient might better be treated by diathermy according to the method advocated by Weve's clinic.[39] The use of Co^{60} or radium as a substitute for x-ray therapy is not within the scope of this paper.

Among the more ingenious but less effective attempts to use radioisotopes in ocular therapy was the injection of At^{211} into a recurrent epithelial cyst of the anterior chamber in an aphakic eye.[2] Astatine is almost a pure α-ray emitter, with a half-life of only seven and one-half hours. The α-particles would not penetrate through the cyst wall, and it was felt that the isotope would destroy the cyst without damaging the rest of the eye. The treatment failed, but the idea remains an intriguing one.

The only unqualified successful use of radioisotopes in therapy in ophthalmology has been with the Sr^{90} applicator, and some might add the use of radon seeds.

Radioisotopes in Experimental Work

The great contribution of radiobiology to ophthalmology has been in the investigative field. In the relatively short time that isotopes have been available our knowledge of physiology, pharmacology, and other basic sciences has been enhanced enormously. The use of isotopes has been especially important in studies of ocular fluids: aqueous dynamics, blood volume, blood flow rates, and tear secretion.

Much of the present understanding of aqueous formation originated with the studies of Kinsey, Grant, and Cogan on the accumulation of Na^{24}, Cl^{38}, and P^{32} in the anterior chambers of experimental animals. It had been shown previously by the same investigators, through the use of heavy water as a tracer, that water in the anterior chamber exchanges with water in the blood stream at a rate of approximately 50 cu. mm. per minute. They then demonstrated that sodium and chloride enter the anterior chamber at a rate equivalent only to 4 cu. mm. per minute of whole aqueous. From this it became apparent that the rate of formation of aqueous is more nearly related to electrolytes than to water. Further work using Na^{24}, well summarized by Dunphy,[20] resulted in two important concepts which completely changed our ideas on aqueous formation. These are the following: 1. A secretory mechanism exists in the ciliary body, and ultrafiltration plays only a minor role in aqueous formation. 2. The nonelectrolytes enter the anterior chamber by diffusion, whereas most of the electrolytes enter by secretion.

These observations aided in the concepts of the formation of the intraocular fluid by Friedenwald[42] and others[43,44,47] and ultimately to the very practical use of acetazolamide (Diamox) in the treatment of glaucoma.

The electrolyte movement in the cornea was also clarified by the use of radioisotopes. Potts and Johnson[45] used P^{32} as phosphate, Na^{24}, I^{131}, and Cs^{134}. They demonstrated that the limbal vascular plexus plays a predominant role in supplying these materials to the cornea. However, a small but significant amount of these substances passed through the anterior and posterior corneal surfaces. Subconjunctival injection allowed only a small proportion of the injected ions to enter the cornea, and this entry was confined to an area quite close to the site of injection.

The effect of x-ray on permeability of the lens was studied through the use of isotopes (Na^{24}, K^{42}, I^{131}, P^{32}) by von Sallmann and Locke.[46] Their experiments do not lend support to the theory that enhanced permeability of the lens or depressed

Figure 2

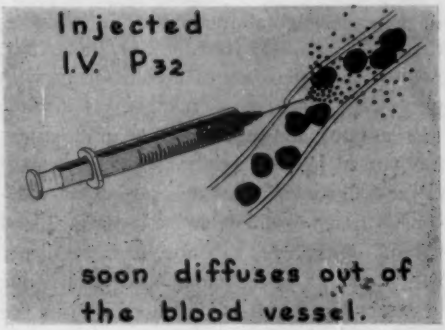

Figure 3

processes of phosphorylation lead to the development of lens opacities by x-rays.

The use of radioautographs permits study of the distribution of many ions within the eye.

We have noted previously that one of the difficulties in using P^{32} in the diagnosis of intraocular melanomas is that its distribution is largely correlated with the vascular supply of the tissue. This very difficulty gives us a new diagnostic tool with which to evaluate the vascularity of the globe and study the effects of drugs and other agents on the intraocular blood volume. P^{32} soon diffuses out of the blood vessels into the surrounding tissue if it is injected intravenously, but if it is incubated into the red blood cells, it then remains within the vascular tree for a long period. This technique consists of withdrawing blood, mixing it with P^{32}, incubating it at 37 C with gentle agitation for two hours, washing the erythrocytes, resuspending them, and then reinjecting them into the animal.[48] The P^{32} is thus completely confined to the erythrocytes, which, in turn, are confined to the vascular tree (Figs. 2 and 3). P^{32} emits only β-particles which travel a maximum of 8 mm. through tissue. If the conjunctiva is removed, a Geiger-Müller tube placed over the sclera posterior to the oraserrata could receive impulses from the following tissues only: the sclera, which contains a negligible volume of blood; the choroid, which contains most of the blood; the retina, with approximately 3% of the blood in the choroid,[49] and the vitreous, which contains no blood. The radioactivity therefore comes from the choroid and retina, and alterations of the blood volume in these structures are reflected in changes of radioactivity (Figs. 4 and 5). This technique, for the first time, permitted a study of agents which affect the blood volume of the choroid and retina

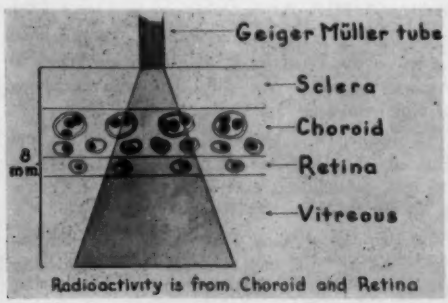

Figure 4

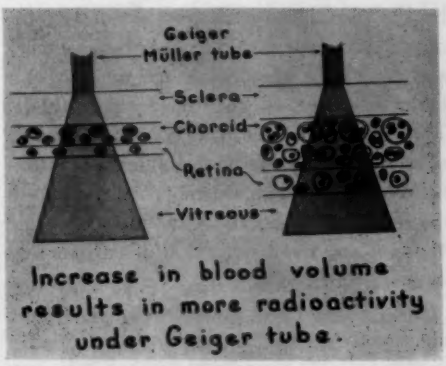

Figure 5

in the experimental animal.[50] The following increased the blood volume: CO_2 inhalation; retrobulbar injections of certain drugs with peripheral actions, notably tolazoline (Priscoline) and aminophylline, and certain mechanical agents, especially paracentesis.[51] Some drugs which produced peripheral vasoconstriction resulted in increased blood volume in the eye; nicotine, in large doses, was one.[52] The technique also allows one to determine the effect of tonography on the intraocular blood volume and whether Grant's formula for the coefficient of aqueous outflow would have to be corrected for this. From my preliminary studies it seems that this effect is negligible.†

It is likely that much of the benefit derived from using radioisotopes in experimental work is still to be felt. This fertile field has already produced a much clearer understanding of ocular physiology, but most of the yield is yet to come.

Summary

The modern ophthalmologist should have a clear concept of isotopes. For most purposes in ophthalmology pure β-ray emitters must be used. Generally, the most useful are Sr^{90} in therapy and P^{32} in diagnosis and much of the experimental work. Radioisotopes in therapy are generally only useful for external therapy as Sr^{90} applicators or radon seeds. P^{32} has been used extensively in the diagnosis of intraocular malignancies, but its usefulness is limited. Radioisotopes are of the greatest help in investigative work and have been responsible for much of our understanding of the intraocular fluids: This includes present concepts of formation of the aqueous, factors influencing intraocular blood volume, the movements of fluids through such ocular tissues as the cornea and the lens, and the distribution of various ions in ocular structures.

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† Bettman, J.; Fellows, V., and Chao, P.: Unpublished data.

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Aniridia and Related Iris Defects

A Report of Twelve Cases with Bilateral Cataract Extraction and Resulting Good Vision in One

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Aniridia or irideremia is a clinical term denoting absence of the iris in whole or in part. Actually, total absence has not been reported, as there has been rudimentary iris tissue in all cases reported in the literature. Because of the ease of investigation, aniridia has been extensively studied by geneticists. Several theories have been advanced to account for this condition, chief among which are the mesodermal theory of Ida Mann [1] and the ectodermal theory. Duke-Elder [2] believes that both are operative, in different cases. Series have been reported which would make the defect appear to be recessive, on the one hand, while other series would indicate that it is dominant. According to Callahan,[3] it is generally inherited from affected members in proportion of approximately 50%. Occasionally a single case is seen in some family where there is no other history of eye disorders; these have been variously ascribed as being due to Mendelian recessive traits linked to cases more remote than our knowledge or to mutations. However the latter possibility, while its existence has been acknowledged, is thought to be extremely rare. The genes producing aniridia also effect various anomalies, such as ectopia lentis, ectopia pupillae, abnormalities of mesodermal and ectodermal defects in the iris, iridotasis, and embryotoxin. Any of these abnormalities in moderate or severe form which follow no certain pattern of distinction would indicate the presence of the gene in the family under study. Cases with ectopia lentis may be children of parents with aniridia and vice versa. The tendency for colobomata and hypoplasia of the iris to occur in aniridic families is frequently noted. Colobomata are usually unilateral while aniridia is most often bilateral, but the frequency with which the two are associated would seem to indicate that aniridia is simply a severer form of coloboma and consequently that the causative mechanism is identical.

Vision is usually poor in cases of aniridia, although not necessarily so. Reasons for this have varied with different writers. Vogt [4] first suggested that it was due to a concomitant absence of the fovea centralis, and this absence has been confirmed histologically by at least one writer (Seefelder [5]). This reason has been given also by Berens [6] and by Duke-Elder.[2] Another explanation, most recently advanced by Alger [7] and attributed to Ishikawa by Friede [8] in 1924, blames the failure of development of the fovea on the lack of stimulation due to the aberration of the light. That there is not absence of the fovea in every case is borne out by the reported cases of good visual acuity, and the theory of poor stimulation of the fovea due to aberration would seem more applicable, although the cases of good visual acuity must be granted to be exceptions to this theory also. Alger advocated the use of corneal tattooing in order to cut down on aberration and reported a case in which he used this method. A corneal ulcer ensued in one eye, but two years later the visual acuity was 20/20 in one eye and "almost as good in the other."

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Reid [9] reported a case in which the fitting of a contact lens which contained an opaque brown corneal portion with a 2.5 mm. pupillary portion improved vision from 6/12 to 6/6. This case was reported in 1938, and, although there have been vast improvements in contact lenses and several makers now advertise cosmetic lenses such as this, there have been no recent reports of this type of management.

A frequent accompaniment of aniridia is glaucoma, and, again, the incidence of this condition has varied according to the writer. Julia Bell [10] says, "It would appear that there is no marked liability to glaucoma in the aniridic patient," but Treacher Collins repeatedly spoke of greater predisposition of aniridic eyes to glaucoma, basing his opinion on histological findings.

Duke-Elder [2] states that secondary glaucoma develops in a considerable proportion of cases, basing it on anatomical defects with a reduction in the available filtration angle. Berens [6] reports the development of glaucoma in 23 of 83 patients. Callahan [3] observed that ectopia lentis seemed to contribute to glaucoma in aniridia, although in cases of ectopia lentis alone glaucoma is uncommon. At the present time it would seem that secondary glaucoma is a danger to be watched for and that its incidence is directly proportional to the amount of open or closed angle in the given case.

Meller [11] and others have proposed the theory that much of the absorption of aqueous is performed by iris crypts and that the lack of this absorptive surface may be another factor in the production of glaucoma, but in view of recent work on the ex-flow of aqueous this factor would seem to be insignificant. Several authors have reported that the secondary glaucoma of aniridia is well controlled with physostigmine (eserine) and advance the theory that the mechanism is one of constriction of the blood vessels since there can be no miosis (Reid,[9] Dennis,[12] and Scolinci). Hudson [13] reported control of tension by corneoscleral trephining in a 7-week-old child with aniridia, and Barkan [14] has advocated goniotomy under direct visualization.

According to Beattie,[15] no satisfactory treatment for the glaucoma has been advanced. Wiener and Alvis [16] state bluntly that operative treatment is hopeless. Callahan [3] reported a complete lack of response to pilocarpine, physostigmine, and similar drugs in his cases, all of which combined aniridia with ectopia lentis. Five of his cases had varying surgical procedures, including goniotomy, trephining, cyclodialysis, flap sclerotomy, and cyclodiathermy. He stated that none was particularly satisfactory and that cyclodiathermy was noted to cause a rise in tension in several cases. He found that the tension curve in the eye not operated on tended to parallel that in the eye operated on and postulated that the relaxation from the general anesthetic might be of more benefit than the surgery. He noted that aniridic eyes seemed to withstand pressure better than normal eyes because there was little field loss over a two-and-one-half-year period in spite of his inability to control the tension. No reports have been made concerning the use of acetazolamide (Diamox) in aniridic glaucoma, but in view of its success in other forms of primary and secondary glaucoma it probably will be helpful in these difficult cases also.

Aniridic eyes not complicated by other abnormalities seem prone to develop cataracts at an early age. The presence of an anterior polar cataract suggested to Treacher Collins [17] that the defect was one due to abnormal and prolonged adhesions of the lens to the cornea. Several cases of cataract extraction in aniridia have been reported, some of which have been successful. Most operators seem to feel that the extracapsular extraction is safer, although one author suggests that intracapsular extraction would produce less reaction. Most extracapsular operations apparently require subsequent capsulotomy or discission. DeBeck [18] reports lens extractions with vitreous loss and subsequent cyclitis. Foster [19] wrote that a number of operators have testified that a

greater degree of cyclitis or other destructive inflammation attends lens removal than is usually the case. He feels that this might be due to the relatively poor vascularity of the anterior segment, having no iris framework for vessels and consequently being less able to absorb foreign protein from the lens and overcome slight infection. Dennis [12] reported cataract extraction of the right eye in a patient with bilateral aniridia. Extracapsular extraction with subsequent discission yielded 6/60 vision. Blue [20] reported bilateral cataract extraction in a 46-year-old man with aniridia. One eye developed an adventitious hyaloid membrane, but the other one achieved 20/40 vision. The most recent of these cases was reported in 1922, and few subsequent reports of cataract extraction in aniridia have appeared.

The cases to be reported in this paper consist of 12 members of one family, comprising three generations. Five cases showed bilateral aniridia; two cases showed colobomata, one bilateral and the other unilateral. Four cases showed minor iris defects, and one case (age 19 months) appeared to have normal eyes. It is interesting to note that the five cases of aniridia occurred in the first and second generations and that the milder iris deformities and the one normal case all occurred in the third generation. Only one member of this group showed glaucoma at the time this study was made; however, she was considerably older than the rest of the group and gonioscopy findings in the other members make it likely that there will be other cases of glaucoma eventually.

Seven members of this series showed lens changes. One had had previous cataract surgery and is now blind with glaucoma; one was operated on bilaterally during this study, with resulting good vision, and the other five showed changes of less degree, not requiring intervention at this time. The cases are reported in chronological and genealogical order.

Report of Cases

CASE 1.—A 49-year-old white woman (first generation), was seen because of pain and blindness in both eyes. Vision was no light perception in the right eye and light perception only in the left eye. She had had a cataract extraction in the right eye in 1945, with a history of good vision for 12 to 18 months and then gradual failure. Vision in the left eye failed gradually, beginning about 1943. This patient had three siblings living with no history of eye defects, and her parents had shown no eye defects.

Examination was as follows: O. D., the cornea was opaque over three-fourths of its surface, with a band keratopathy and a small staphyloma superiorly. There was a membrane across most of the pupillary space, but a very pale optic disc could be seen. O. S., there was band keratopathy with vascularization of the cornea and anterior lens capsule. A hypermature cataract was in situ. With the slit lamp a very narrow band of iris, perhaps 2 mm. wide, could be seen. Tension was 45 mm. Hg O. D. and 55 mm. Hg O. S. (Schiøtz). Pain was intermittent, and the patient had apparently grown accustomed to it, as she complained very little about it. Attempts to lower tension with miotics were unsuccessful.

CASE 2.—A 23-year-old white woman (second generation), daughter of Case 1, had vision of 20/50 O. U. which was not improved by refraction. She complained only of photophobia. Examination revealed

Fig. 1 (Case 2).—Bilateral aniridia.

Fig. 2 (Case 3).—Bilateral aniridia. Aphakic O. S., mature cataract O. D. (In making the photographic print the film was printed from the wrong side, reversing the print).

bilateral aniridia, with the remnants of iris varying from none visible to 2 to 3 mm. in width. In most areas zonules were clearly seen. There were a moderate number of posterior cortical opacities in O. U. appearing as tiny white spots tending to clump together. A few discrete ones were seen anteriorly. Tension was 13.5 mm. Hg O. U. (Schiøtz). Gonioscopy revealed an open angle in all areas O. U. with a normal-appearing trabeculum. Cycloplegic refraction revealed mild myopic astigmatism O. U.

Case 3.—A 21-year-old white woman (second generation), daughter of Case 1. This patient was first seen in 1940 at the age of 7 with a complaint of esotropia, present since the age of 1 year. The esotropia was alternating and not improved by glasses, and the left eye was dominant. Aniridia and bilateral cataracts were noted at that time. Visual acuity was recorded as 20/30 O. U. and improved to 20/20 with correction. A recession of the right medial rectus and advancement of the right lateral rectus muscle was done at that time. Six months later, a modified tenotomy of the left medial rectus was done because of residual esotropia. The patient was not seen again until May 18, 1954, at which time she complained of failing vision in both eyes for the past three to four years. She had a fixed internal strabismus of the left eye, with inability to move the left eye out to the midline. Examination revealed bilateral posterior lamellar cataracts, with an almost mature one O. S. and an earlier one O. D. Vision was L. P. and good projection O. S. and 6/200 in O. D. Tension was 20 mm. Hg O. D. and 23 mm. Hg O. S. (Schiøtz).

Slit-lamp examination revealed an almost mature lens O. S. and posterior cortical lamellar opacities O. D. Fundus could not be seen O. S., but in O. D. it appeared essentially normal except that no foveal reflex could be seen. The anterior chambers were deep, and there were no posterior synechiae. Zonules could be seen on all sides of both lenses, with a small rim of iris tissue, in some areas not exceeding 1.5 mm.

An extracapsular extraction was done on the left eye on June 3, 1954. Surgery was done with use of local anesthesia, and care was taken to remove as much of the capsular material as possible; no vitreous was lost. Recovery was uneventful, and refraction on July 30, 1954, revealed 20/50 vision (20/40 with pinhole). After cataract surgery O. S. the cataract in O. D. matured rapidly, and extraction was done on it on Aug. 25, 1954. Again operation and recovery were uneventful and refraction yielded 20/50 (20/30 with pinhole). In neither eye was a discission required, as both eyes had good central openings in the posterior capsular material.

Because of the strabismus fixus O. S. it was felt that the left lateral rectus was paretic, but because of the history of previous surgery on the left medial rectus, and the possibility of excessive scar tissue binding it down an exploration of the left medial rectus was done first. With use of general anesthesia, a fixed medial rectus was found on forced ductions. It was found to have a 3 to 4 mm. attachment extending almost up to the limbus. This attachment was freed up, and all intermuscular membranes and check ligaments were cut; no abnormal footplates were found. The medial rectus was then recessed 4 mm. and a 5 mm. resection of the left lateral rectus was done. Postoperatively the left eye remained in the primary position with the ability of adduction but the patient still could not abduct the eye past the midline.

Gonioscopy O. D. showed the iris stump adherent to the sclera over the entire circumference except for a very small area temporally, which appeared narrowed but open. Gonioscopy O. S. showed the base of the iris tightly adherent to the sclera everywhere except in two small areas inferiorly, where trabecular structures could be seen. Both of these areas appeared to be only 1 to 2 mm. long. At 12 o'clock the pupillary edge of the narrow iris was folded back and adherent to the sclera. Tension was 23 mm. Hg O. D. and 14.5 mm. Hg O. S. (Schiøtz).

CASE 4.—A 16-year-old girl (second generation), daughter of Case 1, had a visual acuity of 20/200 O. D. and 10/200 O. S. With correction, vision was 20/25 O. U. This patient presented slightly eccentric pupils, with a suggestion of a coloboma in the superior nasal quadrants O. U. Reaction to light and in accommodation was normal. On slit-lamp examination the iris crypts were found to be very shallow, with absence of the pigment fringe temporally and below. Dilation with 10% phenylephrine (Neo-Synephrine) showed poor response but was adequate for ophthalmoscopy, which was normal. Tension after dilation was 20 mm. Hg (Schiøtz) O. U. Gonioscopy O. D. showed open angle with normal-appearing meshwork. In the left eye there were iris strands reflected onto the sclera but many openings into the angle, and so no significant impairment of drainage should result.

CASE 5.—A 12-year-old girl (second generation), daughter of Case 1, had vision of 20/60 O. D. and 20/50 O. S. With correction vision was 20/50 O. D. and 20/40 O. S. (hyperopic). This child presented aniridia O. U., with only 1 to 2 mm. of iris tissue in any area. Inferiorly O. D. there appeared to be no iris at all. The lenses were grossly clear and showed normal architecture, but there were a few scattered white opacities in the posterior cortex and rare ones in the anterior cortex peripherally. Vitreous was clear, and the fundus appeared normal. No foveal reflex could be seen in either eye. Gonioscopy showed the angle to be open widely in all areas in both eyes, with a normal-appearing trabeculum.

Fig. 3 (Case 7).—Coloboma O. D. Hyperplasia O. S.

CASE 6.—A 9-year-old girl (second generation), daughter of Case 1, had vision of 20/50 O. U. correctible to 20/40 (hyperopic astigmatism). There were no history of eye complaints and no photophobia. This patient also presented aniridia O. U. The lenses showed normal architecture, with a few scattered white spots in posterior cortex peripherally, more marked in O. S. Vitreous and fundus were normal except for the absence of foveal reflexes. Gonioscopy revealed very little angle in any area of either eye. The iris root seemed to come right up to the sclera, with only an occasional opening into the angle.

CASE 7.—A 6-year-old white boy (third generation), son of Case 2, presented rotary nystagmus, present since birth. Examination showed a coloboma of the iris at 5 o'clock O. D. The iris was smooth, with lack of cryptic structure, and a few discrete white spots were seen in the posterior cortex of the lens. In the left eye the pupil was intact but iris structure was flattened and there was absence of surface layer and color at 3 o'clock. Ophthalmoscopy and tension were normal.

Gonioscopy showed an open angle in all areas, with a normal-appearing trabecular meshwork. Cycloplegic refraction showed a hyperopic astigmatism.

CASE 8.—A 4-year-old boy (third generation), son of Case 2, presented a hori-

Fig. 4 (Case 8).—Coloboma 9 o'clock O. D. Coloboma 3 o'clock O. S. (The print is reversed).

zontal nystagmus of the fixation type. Examination revealed a coloboma of the iris at 9 o'clock O. D. and at 3 o'clock O. S. The lenses were clear. Refraction showed hyperopic astigmatism. Fundus and intraocular tension were normal. Gonioscopy showed an open angle in all areas.

CASE 9.—A 3-year-old boy (third generation), son of Case 2, had pupils that were round, regular, and equal and that reacted normally to light. Pupils dilated well, and iris structure appeared flattened, with loss of crypts. There was a tiny posterior central lens opacity O. U. Cycloplegic refraction showed a mild myopia O. U.

CASE 10.—A one-year-old boy (third generation), son of Case 2, had pupils that were round, regular, and equal and that reacted normally to light. Iris structure was smooth, with loss of surface crypts, and in the left eye there was an area temporally where the superficial layer was absent. Lenses were clear. Cycloplegic refraction showed hyperopic astigmatism.

CASE 11.—A one-month-old girl (third generation), daughter of Case 2, had bilateral iris defects at 11 o'clock O. D. and at 2 o'clock O. S., with thinning of the iris and absence of the superficial layer. Lenses appeared clear.

CASE 12.—A 19-month-old girl (third generation), daughter of Case 3, had no defect of the iris or lens.

Comment

The spontaneous appearance of aniridia in the oldest member of this group and the absence of any known eye defects in her siblings and parents would seem to indicate an origin by mutation. The explanation of a Mendelian recessive would not be applicable in view of the appearance in a dominant fashion in the second generation (four out of five showed aniridia). All defects occurring in the first and second generation concerned the iris and lens both, except for the one case with only slightly eccentric pupils; she showed no lens changes. None of this series exhibited ectopia lentis, and only three of the entire group exhibited extraocular deformities. (Two had nystagmus, and one case showed esotropia, which

Summary of Findings in Twelve Members of One Family with Aniridia and Related Iris Defects

Case	Age, Yr.	Extraocular Defects	Vision	Ref. Error	Iris Defects	Lens Changes	Gonioscopy	Glaucoma
1	49	None	O. D. blind O. S. L. P.	Unknown	Aniridia O. U.	Cataracts O. U.,	Not possible	Yes, O. U., uncontrolled
2	23	None	O. D. 20/50 O. S. 20/50	Myopic astig.	Aniridia O. U.	Posterior cortical opacities	Angle open in all areas	No, not anticipated
3	21	Esot.	O. U. 20/30	Aphakic	Aniridia O. U.	Cataracts O. U.	Angle largely occluded	No, but expected
4	16	None	O. U. 20/25	Myopia	Eccentric pupils, hypoplasia	None	Angle open	No, not anticipated
5	12	None	O. D. 20/50 O. S. 20/40	Hyperopic astig.	Aniridia O. U.	Posterior cortical opacities	Angle open	No, not anticipated
6	9	None	O. D. 20/40 O. S. 20/50	Hyperopic astig.	Aniridia O. U.	Posterior cortical opacities	Angle 80% to 90% blocked	No, but expected
7	6	Rotary nystagmus	O. D. 20/200 O. S. 20/200	Hyperopic astig.	Coloboma O. U., hypoplasia	Posterior cortical opacities	Angle open	No, not anticipated
8	4	Horizontal nystagmus	O. U. 20/200	Hyperopia	Coloboma O. U.	None	Angle open	No, not anticipated
9	3	None	Undet.	Myopia	Hypoplasia	Tiny central opacity	Not done	No
10	1	None	Undet.	Hyperopic astig.	Hypoplasia	None	Not done	No
11	1 mo.	None	Undet.	Hyperopic astig.	Mild colobomata O. U.	None	Not done	No
12	19 mo.	None	Undet.	None	Mild colobomata O. U.	None	Not done	No

is not thought to be related to the intraocular defects.) In general, visual acuity was very good in this group. In several of the younger children no measurement of the visual acuity could be made, but, except for the two with nystagmus, there is no reason to believe that their vision will be worse than that of the other members showing greater defects. Vision in all of those showing aniridia was 20/50 or better except for the oldest member, who is now blind, and in her case vision was apparently very good until the development of cataracts and glaucoma.

In view of visual acuity of 20/50 or better, the theory of aplasia or absence of the fovea would not be acceptable in this series, and the theory of poor stimulation of the fovea and macular area due to aberration and dispersion of light would seem more plausible. The reason for visual acuity of 20/20 O. U. in the one case at age 7 would not be apparent no matter what the explanation for poor vision in the other cases might be. Certainly there is no correlation in this case between the vision and the amount of iris tissue present, because this patient had as little iris as any patient in the group.

Correction of visual acuity by tattooing, as recommended by Alger, was considered but was dismissed because of the possible complications. This method is condemned by other writers and would seem unduly hazardous in young patients with bilateral aniridia. Cosmetic contact lenses would be a safer method of accomplishing the same thing, although they cannot be fitted at a very early age. An attempt was made to have the cataract patient in this group fitted with cosmetic contact lenses, but she was not sufficiently interested in them to carry out the fitting procedure. There would not appear to be any correlation between the congenital defects and refractive errors, as three patients showed myopia, five showed hyperopia, and in two cases the refractive error was insignificant. Anterior chambers were deep in all cases, and in none was there any evidence of uveitis. Only one case showed glaucoma at the time this study was made, and she had had it for a number of years. Her tension varied from 40 to 60 mm. Hg (Schiøtz); she had very little pain, however, and refused to use miotics because of the discomfort they caused. There was no indication that miotics influenced her tension, however, during the time when she did use them. Among the other members of the group, only two cases showed significant blockage of the angle. One of these was the case operated on for cataracts, and the other was a younger sister; in both cases aniridia was present. Both of these exhibited normal tensions during the time they were under observation but, because of the amount of blockage of their chamber angles, it is highly probable that they will develop glaucoma at some future date. The other members, all showing open and normal-appearing angles, would seem no more prone to develop glaucoma than any patient with normal eyes. Anterior synechiae would probably form more easily in cases of aniridia because of the frailty of the iris stump, and it is possible that minimal attacks of uveitis may be responsible for these synechiae.

Since the development of glaucoma, while fairly common in aniridia, hinges on the amount of functioning angle which may be directly observed gonioscopically, it should be possible to predict with a fair measure of success in all cases whether glaucoma is likely to ensue.

Treatment of glaucoma in the aniridic patient is a particularly trying problem. Practically every method of treatment known has been advocated by at least one author and condemned by another. The best method would seem to hinge on early diagnosis and conservative management. Barkan [14] has advocated goniotomy in cases occurring in children and likens the problem to that of ordinary congenital glaucoma. He, too, stresses the importance of early diagnosis and feels that long-standing increased pressure causes obliteration of

Schlemm's canal, after which no treatment is effective. Cyclodiathermy would seem to offer a good method of approach, but Callahan's series indicates no benefit from this procedure; indeed, it seemed to aggravate the glaucoma in several cases. As mentioned earlier, acetazolamide may offer satisfactory treatment for these difficult cases and certainly should be tried prior to the various surgical procedures. The development of cataracts is another complication which is fairly common in aniridia. Two cases of this group had developed opacities impairing vision sufficiently to necessitate cataract extraction. In addition, five others exhibited varying degrees of lens opacities. In all cases these were posterior cortical and appeared as numerous tiny white specks. Their location in the posterior cortex would rule out the possibility of their being caused by abnormal and prolonged adhesions of the lens to the cornea, as advanced by Treacher Collins.

In the case operated on bilaterally during this study, no operative or postoperative complications were observed; the eye healed and progressed just as any normal eye. The absence of iris and the prominence of the zonules and the vitreous would seem to contraindicate intracapsular extraction. In addition, it is likely that most such cataract surgery will be done on relatively young persons, where the zonules are tougher and the chance of rupture of the capsule is greater. For these reasons, extracapsular extraction would seem to be the method of choice. I believe that any increase in the degree of cyclitic reaction postoperatively can be controlled by the use of steroids, although this is not recommended routinely in extracapsular extractions, as their use tends to inhibit the absorption of lens material. The indications for cataract surgery in cases of aniridia should therefore be judged on an individual basis just as in any other cataract surgery, and the presence of aniridia should not unduly deter the surgeon.

Summary

A series, comprised of 12 members of one family, encompassing three generations, with aniridia and related iris defects in 11, is presented. The mechanism of causation is discussed along with the complications which are attendant. Bilateral extracapsular cataract extraction in one case, with resulting good vision, is reported. The treatment of glaucoma and the management of cataracts in aniridia are discussed.

105 E. Pitkin St.

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Acetazolamide (Diamox) Therapy in Chronic Glaucoma

A Three-Year Follow-Up Study

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Since 1954, when acetazolamide (Diamox) * became available as an additional therapeutic agent for the management of glaucoma, several reports dealing with long-term acetazolamide therapy in chronic glaucoma have been published.[1-8] A variety of hypotheses have been advanced concerning the mode of action of this drug.[9-15] At the present time, all that can be said with certainty is that acetazolamide is a specific carbonic anhydrase inhibitor, that it lowers intraocular pressure of human and animal eyes, and that it does so by a partial inhibition of aqueous humor formation. The mechanism of action of this drug as well as its exact locus of action still remains to be demonstrated. Since carbonic anhydrase is known to be present in lens epithelium, ciliary body, and retina, it became of immediate interest to study two main problems: (*a*) Does long-term administration of acetazolamide interfere with the metabolic processes of ocular tissues? (*b*) Will the prolonged administration of acetazolamide irreversibly suppress the process of aqueous formation, i. e., produce a "biochemical cyclodiathermy"?

This report deals with two general aspects: (1) the effect of two or three years of continuous acetazolamide and miotic therapy on the aqueous dynamics of glaucomatous eyes and (2) a critical evaluation of the clinical status of patients maintained on long-term acetazolamide and miotic therapy.

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Methods and Material

All of our patients were drawn from the general glaucoma clinic of the Wilmer Institute and were studied in the Diamox Research Clinic which was started in 1953 by the late Dr. Jonas S. Friedenwald. The present study covers the period from October, 1953, to February, 1957. Fifty-nine per cent of the patients studied had had one or more filtering operations with subsequent uncontrolled tensions prior to their admission to the Diamox Research Clinic. Forty-one per cent had had no previous surgery but their tensions could not be controlled on maximal medial therapy and they were therefore referred to the Diamox Research Clinic.

All patients in this series were maintained on pilocarpine, 2% to 7%, 0.25% physostigmine five times daily in addition to ointment at bedtime, and some patients were also given 0.1% isoflurophate once daily. In addition, they received an average dose of 1.0 gm. of acetazolamide a day, given in divided doses of 250 mg. four times a day.

Follow-up visits occurred at six- to eight-week intervals. A complete blood cell count and urinalysis were performed at regular intervals, and an abdominal flat plate x-ray was obtained at the end of the study on all patients who had been maintained with acet-

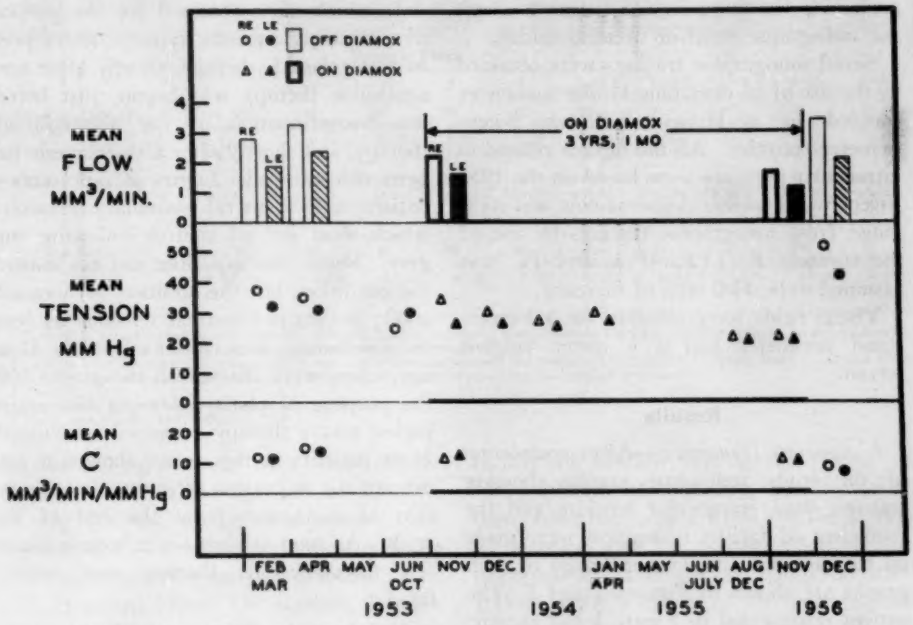

Fig. 1 (Case 21).—Case of a 47-year-old Negro woman with simple glaucoma.

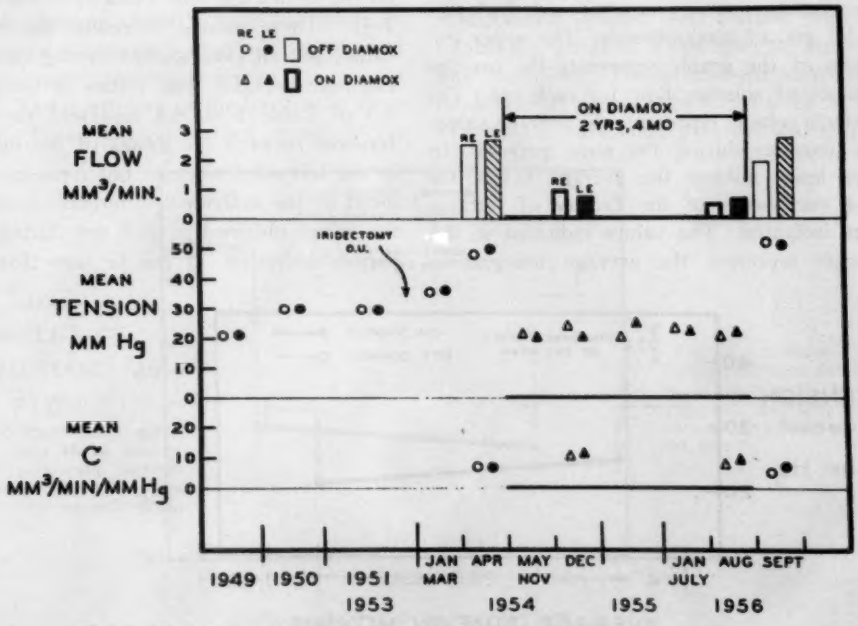

Fig. 2 (Case 15).—Case of a 51-year-old woman with secondary glaucoma.

azolamide for two years or longer to check for radiopaque renal or ureteral calculi.

Serial tonographic tracings were obtained by the use of an electronic Muller tonometer coupled to a Honeywell-Brown potentiometer recorder. All the figures related to intraocular pressure were based on the 1954 Friedenwald tables. Aqueous flow was computed from tonographic tracings by use of the formula $F=C(P_o-P_v)$, and P_v, was assumed to be 11.0 mm. of mercury.

Visual fields were obtained on a Ferree-Rand perimeter and a 1 meter tangent screen.

Results

1. Aqueous Dynamics.—After completion of the study individual graphs showing aqueous flow, intraocular tension, and the coefficient of facility of outflow were made up for each patient. Two examples of such graphs are shown in Figures 1 and 2. The patient represented in Figure 1 had chronic simple open-angle glaucoma. His tensions were inadequately controlled by miotics, and so acetazolamide therapy was begun in October, 1953. This treatment was continued for just over three years, with a daily dosage of 1 gm. of acetazolamide. The upper column of the graph represents the average values of aqueous flow for each eye. The middle column represents the average values of tensions during the same periods. In the lower column the average values for the coefficients of the facility of outflow are indicated. The values indicated in the graph represent the average tonographic data which were obtained for the purpose of comparing aqueous dynamic states prior to acetazolamide therapy, shortly after acetazolamide therapy was begun, just before the discontinuation of the acetazolamide therapy, and shortly after acetazolamide had been discontinued. Figure 2 represents a patient with bilateral secondary glaucoma which went out of control following surgery. Miotic therapy alone did not control the condition, but the addition of acetazolamide maintained normal tensions as long as this therapy was continued. Only average values were charted on the graphs, for the purpose of clarity. During this entire period miotic therapy remained unchanged. Most patients in this series showed a significant rise in tension after the discontinuation of acetazolamide at the end of the study. As soon as such a rise became manifest, acetazolamide therapy was reinstituted.

A. Intraocular Tension: In Figure 3 the average values for ocular tensions for the four periods under study are represented graphically. The graph in Figure 3 is based on the values listed in Table 1,B (Columns 1-4). These values represent the mean values for all eyes studied during each of the four periods. The values in Columns 5-9 of Table 1 do not represent the differences between the means of the figures in the left-sided columns but represent the mean of the individual differences between the values obtained in each eye during the periods indicated. It can be seen that the

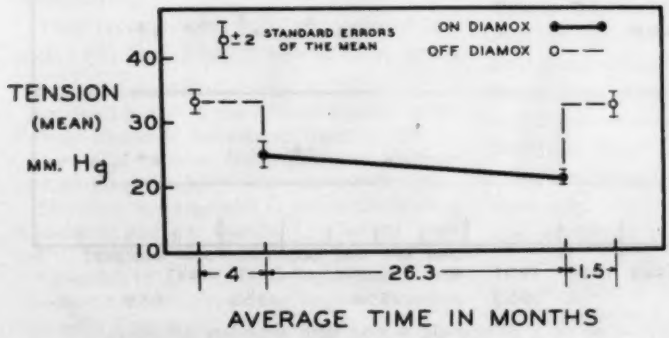

Fig. 3.—Average ocular tension in 44 eyes with chronic glaucoma, with and without acetazolamide therapy.

TABLE 1.—*Summary of Aqueous Dynamics Data*

		Period of Therapy *								
		1	2	3	4	1–2 †	1–3	1–4	4–3	2–3
A. Aqueous Flow (F),‡ cu. mm.³/min.	Eyes, No.	36	36	38	43	29	31	36	38	36
	Mean	1.62	0.94	0.69	1.45	+0.93	+1.05	+0.26	+0.80	+0.23
	S. D.	0.14	0.15	0.10	0.13	0.14	0.13	0.15	0.11	0.12
	P §					<0.001	<0.001		<0.001	
B. Tension,‖ mm. Hg	Eyes, No.	44	44	44	44	44	44	44	44	44
	Mean	35.10	24.01	22.23	34.70	+11.16	+12.98	+ 0.43	+12.55	+1.36
	S. D.	1.42	1.32	0.88	1.52	2.03	1.62	1.49	1.36	1.14
	P					<0.001	<0.001		<0.001	
C. Outflow facility (C), cu. mm.³/min./mm. Hg	Eyes, No.	36	36	38	43	31	31	36	38	36
	Mean	0.095	0.099	0.091	0.074	+0.003	+0.011	+0.021	+0.013	+0.010
	S. D.	0.008	0.009	0.008	0.007	0.007	0.007	0.006	0.006	0.006
	P							<0.001	<0.05	

* Column 1, before acetazolamide therapy; Column 2, after beginning acetazolamide therapy; Column 3, prior to stopping acetazolamide therapy; Column 4, after stopping acetazolamide therapy.
† Column 1 — Column 2; this does not represent the differences between the means of the figures in Columns 1 and 2, but the mean of the individual differences between the values obtained in each eye during the periods indicated.
‡ $F = C(P_o - 11.0)$.
§ Probability is listed where difference was significant.
‖ From 1954 Friedenwald tables.

tension fell significantly with acetazolamide therapy, with an average fall of 12 mm. of Hg for the group as a whole. The tension rose to essentially pretherapy levels after acetazolamide was discontinued.

B. Aqueous Flow: The aqueous flow decreased significantly as a result of acetazolamide administration (Table 1,A and Fig. 4). The average flow reduction of aqueous with acetazolamide was 60% in comparison with the average flow prior to acetazolamide administration. Shortly after cessation of acetazolamide therapy aqueous flow returned to essentially pretherapy levels.

C. The Coefficient of the Facility of Outflow: There was no marked change in the facility of outflow during the period of study (Table 1,C and Fig. 5). However, there appeared to be a trend for the facility to decrease with the passage of time and, unexpectedly, the greatest drop occurred following the cessation of the acetazolamide therapy. This drop in the facility of outflow after the discontinuation of long-term acetazolamide therapy needs further evaluation, and we shall elaborate on it in the comment below.

II. Clinical Studies.—A. Tension Control (Table 2): In 21 of 24 patients the tension was controlled. The breakdown according to number of eyes was as follows: In 32 of 44 eyes the intraocular pressure was main-

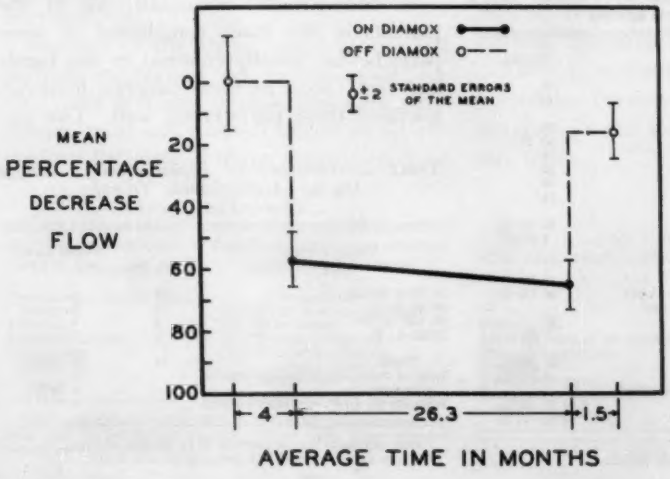

Fig. 4.—Average percentage decrease of flow in 38 eyes with chronic glaucoma, with and without acetazolamide therapy.

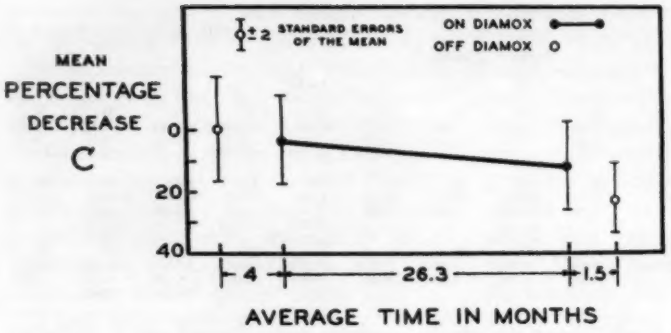

Fig. 5.—Average percentage decrease in outflow facility in 38 eyes with chronic glaucoma, with and without acetazolamide therapy.

tained at 24 mm. Hg (Schiøtz) or less (1954 Friedenwald tables); 10 of 44 eyes had an intraocular pressure between 24 and 33 mm. Hg, and only 2 of 44 eyes had pressures greater than 30 mm. Hg. In these two eyes the tensions rose even further when acetazolamide was discontinued. In 4 of 44 eyes surgery was required after acetazolamide therapy was started; however, postoperative tension control was obtained only with the addition of acetazolamide.

B. Visual Acuity (Table 3): Twenty-five per cent of the eyes studied lost some vision, but in only nine per cent (4 of 44 eyes) could the loss of vision be attributed primarily to glaucoma. Among the four eyes which lost some vision; in two the vision prior to acetazolamide therapy was 20/20; in one, 20/50, and in one, 20/100.

C. Visual Fields (Tables 4 and 5): Only 30 eyes had satisfactory visual field examinations for comparative evaluation. Of these, eight eyes lost at least 15 degrees of field in some meridian. Of the eight that lost field, six had fields greater than 50 degrees (maximum diameter) with the 3/330 or 6/330 white test object on the Ferree-Rand perimeter and four had full fields. Six of the eight which lost visual field had tensions of less than 24 mm. Hg.

D. Ocular Complications: There was no evidence of any permanent ocular complication resulting from acetazolamide administration. A listing of incidental cataracts, uveitis, and other conditions occurring in this series is included in the Appendix.

E. Side-Effects: Practically all of the patients in this study complained of some paresthesias, usually confined to the hands and feet. Most of these patients, however, tolerated these paresthesias well. Two pa-

TABLE 2.—*Summary of Data of Patients Given Acetazolamide Therapy*

	Values
Patients, No.	24
Eyes, No.	44
Age, yr.	
Mean	54
Range	30-75
Whites, No.	4
Negroes, No.	20
Men, No.	10
Women, No.	14
Type of glaucoma, No. of eyes	
Simple (open-angle)	40 (91%)
Secondary	4 (9%)
Approximate duration of glaucoma, yr.	
Mean	7
Range	1-20
Surgery prior to acetazolamide, no. of eyes	26 (59%)
Duration of acetazolamide therapy, mo.	
Mean	27
Range	5-38
Tension, No. of patients	
Controlled *	21 (87%)
Uncontrolled	3 (13%)
Progressive visual field loss with controlled tensions, no. of eyes	6 of 28 (21%)
Over-all percentage of failures	13%—21%

* Tension of 25 mm. Hg or less (1954 tables).

TABLE 3.—*Summary of Visual Acuity Changes During Acetazolamide Therapy (Forty-Four Eyes)*

Vision Prior to Acetazolamide Therapy	Eyes, No.	Visual Loss,* No. of Eyes
20/30 or better	25	4
20/40-20/70	10	3
20/100-10/200	4	3
5/200-L. P.	5	1
Total	44	11 (25%)
Loss of vision attributed primarily glaucoma		4 (9%)
Initially N. L. P. or anophthalmos		4†

* One complete line or more on 20 ft. Snellen chart.
† These four eyes were not included in this study.

TABLE 4.—*Summary of Visual Field Changes During Diamox Therapy (Thirty Eyes)*

	Eyes	
	No.	%
No change	22	73
Field loss	8	27
8 eyes with field loss *		
Tension uncontrolled	2	
Tension controlled	6	21 (6/28)
Degrees of field loss (diameter)		
Mean		25
Range		15-30

Subdivision According to Initial Field Groups

		Field Loss	
Group	Eyes, No.	Eyes, No.	Eyes with Tension Uncontrolled No.
I	12	4	1
II	12	2	0
III	6	2	1
Total	30	8	2

* Loss of more than 15 degrees.

TABLE 5.—*Visual Fields Just Prior to Acetazolamide Therapy*

Group	Visual Field Examination *	Eyes, No.
I	Full peripheral fields; central fields revealed no more than a small Bjerrum scotoma	12
II	Peripheral fields not full but greater than 50 degrees in diameter along meridian revealing maximum contraction	12
III	Peripheral fields less than 50 degrees but more than 5 degrees in diameter	6

* Ferree-Rand Perimeter (3 or 6/330/w) for peripheral fields.

tients complained of anorexia and nausea, dyspnea, or excessive fatigue. In one patient acetazolamide had to be discontinued because of marked progressive weight loss. In three patients the total white cell count at the end of the study was below 4000 cells per cubic millimeter.

F. Renal Calcinosis: Recently there have been reports of dysuria and ureteral colic associated with acetazolamide administration.[6] It has also been reported that renal calcinosis can be produced in rats by the administration of acetazolamide.[16] This effect in rats appears to be associated with a significant reduction in the urinary citrate excretion.

Because of the above considerations, all patients maintained on acetazolamide for two years or longer were screened for radiopaque renal and ureteral calculi by an abdominal flat plate. Fifteen patients received such x-ray screening at the end of the study. One patient was found to have a ureteral calculus but was clinically asymptomatic. Another patient had acute ureteral colic while taking acetazolamide and subsequently passed a calculus. In neither one of these patients was there any proof that the condition did not exist prior to acetazolamide administration. One patient followed in our clinic, as a control, had acute renal colic necessitating hospitalization. He was only given miotic therapy and had never received any acetazolamide. The incidence of asymptomatic renal or ureteral calculi in the general population varies with geographical location, humidity, and other factors, and the exact incidence is not known. There is a report that asymptomatic calculi were found in 30% of a clinic population.[17] Even if this figure should prove to be excessively high, it is apparent that, at the present time, we have no clinical evidence which would clearly indicate a causal relationship between acetazolamide therapy and calculus formation.

Table 6 summarizes the side-effects reported by previous investigators. Table 7 summarizes the side-effects encountered in our series.

TABLE 6.—*Side-Effects in Previous Reports* *

Frequent	Rare
Paresthesias, usually well tolerated	Severe acidosis
Anorexia	Dysuria or ureteral colic
Excessive fatigue	Skin rashes
Weight loss	Transient myopia
	Thrombocytopenia
	Agranulocytosis
	Drug fever

* Side-effects occurred in 25% to 33% of all patients receiving long-term acetazolamide therapy. They were more frequent among private patients.

TABLE 7.—*Side-Effects in the Present Series*

	Patients, No.
Paresthesias	12
Anorexia, nausea, or vomiting	2
Marked weight loss	1 *
Dyspnea	2
Excessive fatigue	3
Temporary depression of peripheral white cell count	1

* Acetazolamide therapy had to be discontinued.

Comment

There are several points in this study which deserve further comment. First of all, it can now be safely stated, on the basis of reports by previous investigators and the present three-year follow-up study, that acetazolamide is an effective adjunct in the therapy of chronic glaucoma. In 87% of the patients studied the ocular tension was controlled by the addition of acetazolamide to miotic therapy where miotics alone had failed. Moreover, 59% of all patients had had prior unsuccessful surgery. Preservation of vision and visual fields was achieved in most of the eyes in a group that would otherwise have a very poor prognosis. Serious systemic side-effects in this series were few, and most patients tolerated the drug well. It should be pointed out, however, that all the subjects were clinic patients, and it has generally been observed that private patients in office practice are more difficult to maintain on long-term acetazolamide therapy because of severer subjective side-effects.

The second conclusion which can be derived from this study is that no irreversible suppression of aqueous formation is produced by long-term acetazolamide therapy, at least not during the first three years. As soon as acetazolamide is discontinued aqueous flow—as measured by tonograph—returns to essentially pretherapy levels (Fig. 4). In this connection, a recent study by Langham [15] is of special interest. Using the fluorescein-appearance-time method, he found that, in rabbits, aqueous flow returned to essentially pretherapy levels within six hours in spite of the fact that acetazolamide administration was continuously maintained and intraocular pressure remained reduced. If these findings can be confirmed, they will be of unusual interest, particularly with reference to the possible mechanism of action of acetazolamide in lowering intraocular pressure. Certainly, from tonographic studies in humans we find no evidence of rapid restoration of aqueous flow while the patient is being maintained with adequate doses of acetazolamide, provided that he is responsive to the drug. Neither is there any convincing evidence that acetazolamide, per se, significantly alters ocular rigidity or episcleral venous pressure.

An unexpected finding was a small but significant reduction in the facility of outflow after discontinuation of long-term acetazolamide therapy (Fig. 5). This may indicate the possibility that during long-term acetazolamide therapy there is a trend for the facility of outflow to become slightly greater or at least not to change significantly and that as soon as acetazolamide is discontinued this maintenance of the facility is altered in such a way as to manifest itself in a further reduction of the facility of outflow. Another possibility is that this reduction in facility after discontinuation of acetazolamide may represent some aspect of the peculiar physiology of glaucomatous eyes. A suggestion along these lines has recently been made by Weekers et al.,[16] who found that in a group of glaucoma patients with initially high tensions (44 to 63 mm. Hg) acetazolamide increased the facility of outflow 40%. This change, however, did not occur in eyes with initial tensions of 22 to 38 mm. Hg. These authors feel that in eyes with relatively high tension there is compression of the trabeculae in addition to the preexisting impairment of outflow drainage. As soon as aqueous inflow is partially suppressed by acetazolamide and tension begins to fall, the compression of the trabeculae is relieved, and thus some increase in the facility of outflow occurs.

Pursuing this line of reasoning a little further, one might suppose that in our series (Fig. 5) the facility of outflow dropped after discontinuation of acetazolamide therapy at the end of the study because trabecular compression occurred, owing to a renewed rise in tension. It should be noted, however, that Weeker's studies were of short-term acetazolamide administration while in the series reported here we are dealing with long-term therapy. Nevertheless, if there is a "trabecular compression

factor" in high-tension open-angle glaucoma, acetazolamide could certainly be expected to exert some, although indirect, effect on the facility of outflow. Another explanation for the small change in facility observed in this study may be the possibility that it merely represents an inherent error in the calibration tables employed in tonographic calculations. This latter explanation would appear to be the more plausible one with respect to our patients, since most of them did not have tension as high as in Weeker's group, which ranged from 44 to 63 mm. Hg.

With respect to the locus of action of acetazolamide, Holmberg[19] recently published some very interesting studies of cytomembranes of the ciliary epithelium in rabbits by means of electron microscopy. These newly discovered β-cytomembranes are intracellular structures of the nonpigmented epithelial cells of the ciliary body. The membranes lie immediately underneath the basement membrane and can often be seen in contact with the posterior chamber. These metabolically active cytomembranes may be the site of highly active and specific enzymes which partake in the transformation of tissue fluid to aqueous humor. Holmberg reaches the conclusion, based on observed and photographed changes in the ultrastructure of the epithelial cells, that acetazolamide produces a blockage in the β-cytomembranes which leads to a reduced production of aqueous humor. His studies, however, do not enable him to decide in what manner acetazolamide acts chemically on the cytomembrane.

With respect to visual fields (Table 4), we found in this series that in 6 of 28 eyes there was significant progressive visual field loss in spite of controlled ocular tensions. Three of these six eyes had fields classified under Group I (Table 5), i. e., eyes which had essentially full fields prior to acetazolamide therapy. Ocular rigidities in these eyes were within normal limits. The problem of progressive visual field loss, in face of controlled intraocular pressure, deserves further careful study. To date there are conflicting reports on this particular subject.[20-22]

Regarding the type and dosage of acetazolamide, it has been our experience that the regular 250 mg. acetazolamide tablets (uncoated) are the most effective. They are given in divided doses four times a day or, preferably, every six hours. The average dosage is 1.0 gm. per day, though in many patients the tension can be controlled on smaller doses.

A word of warning is in order in any discussion of acetazolamide therapy. This study concerned itself solely with chronic or simple open-angle glaucoma. None of our patients had acute closed-angle glaucoma. As has recently been emphasized by Becker,[23] Breinin,[24] Chandler,[25] and others, the treatment of acute congestive or closed-angle glaucoma is surgery, although acetazolamide can often be effectively used in the immediate preoperative period so as to provide more favorable conditions at the time of surgery. It cannot be overemphasized that normalization of tension by acetazolamide in acute closed-angle glaucoma should not mislead the ophthalmologist into thinking that surgery can then be indefinitely postponed.

A three-year follow-up is still too short a period to permit a full evaluation of all the toxic effects of a drug such as acetazolamide. We therefore believe that, until longer follow-up studies are available, it is advisable to defer the use of long-term acetazolamide therapy, in chronic glaucoma, until the various local therapeutic agents have proved inadequate. It should then be used as an adjunct to other therapeutic measures and not as a substitute. It would also seem more logical—at least at the present state of our knowledge—to use long-term acetazolamide and miotic therapy in the older age groups with chronic glaucoma rather than in the young. At the time of writing this report, the cost of acetazolamide to a patient taking 1.0 gm. a day is approximately $173.00 per year.

Summary and Conclusions

Of 24 patients with chronic open-angle glaucoma, uncontrolled by maximal medical therapy, 21 (87%) had controlled intraocular pressures over a three-year period of acetazolamide (Diamox) and miotic therapy. The average reduction in pressure was 12 mm. Hg, and the lowered pressure was primarily due to a reduction of aqueous flow (average 60%) as measured by tonography.

The over-all percentage of failures in this series of clinic patients was 13% to 21%; 6 of 28 eyes (21%) revealed progressive visual field loss in spite of controlled intraocular pressure.

The exact site and mode of action of acetazolamide still remains to be established, but there is no evidence that long-term acetazolamide therapy irreversibly suppresses the formation of aqueous humor. Following discontinuation of long-term acetazolamide therapy, the intraocular pressure rose to essentially pretherapy levels. The longest follow-up of continuous acetazolamide therapy in this series was 38 months.

Acetazolamide appears to be a relatively safe drug. Mild paresthesias occur in at least 50% of all patients. Moderate or severe side-effects occur but are rare in our experience. No significant ocular complications occurred. Vision and visual fields were maintained in many eyes where the prognosis would have been poor without the addition of acetazolamide therapy.

Until longer follow-up studies are available, it is advisable to defer the use of long-term acetazolamide therapy until the various local therapeutic agents have proven inadequate. It should then be used as an adjunct to other therapeutic measures and not as a substitute.

It cannot be overemphasized that this study deals solely with chronic simple glaucoma. Except during the immediate preoperative period, acetazolamide therapy has no place in the management of acute, congestive, or closed-angle glaucoma.

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Appendix

Summary of Clinical Data of Patients Receiving Acetazolamide

Case	Age, Yr.	Race	Sex	Approx. Duration of Glaucoma,* Yr.	Other Ocular Conditions †	Surgery Prior to Acetazolamide Therapy	Systemic Conditions	Duration of Acetazolamide Therapy, Yr.
1	50	N	M	3½	Incipient senile cataract R. E.	Yes, O. U.	Lye burns on face; latent syphilis	2½
2	56	N	M	3	None	Yes, O. U.	Peptic ulcer, H. O. V. D.	1
3	72	W	F	5	None	None	Conduction deafness	1
4	59	N	F	3	Preexisting & progressive cataracts	Yes, O. U.	Latent syphilis	2
5	51	N	F	9	None	Yes, O. U.	None	2¾
6	42	N	F	3	None	None	None	2
7	75	W	F	8	Band keratopathy R. E., vitreous hemorrhage L. E.	Yes, O. U.	Hypertension	2¼
8	44	N	F	8 ‡	Old uveitis O. U.	Yes, R. E.	None	3
9	46	N	M	14	High myopia	Yes, L. E.	Latent syphilis	2¼
10	75	N	F	5	Senile cataracts	None	Arteriosclerotic heart disease	2½
11	72	N	F	2	Senile cataracts, senile macular degeneration	None	Latent syphilis	2
12	35	N	M	20	Vitreous hemorrhages R. E.	Yes, O. U.	Congenital syphilis	3
13	60	N	M	10 ‡	Penetrating injury	Yes, L. E.	None	3
14	69	N	M	12	Nuclear sclerosis	Yes, R. E.	Latent syphilis	1
15	61	N	F	10 ‡	Nongranulomatous iritis	Yes, O. U.	Marie-Strumpel's disease	2½
16	51	N	F	1	Nuclear sclerosis, O. U.	None	Cholelithiasis	½
17	72	W	M	1	Nuclear sclerosis, O. U.	None	Hypertension	¾
18	45	N	M	14	Keratinization of conjunctiva, pannus, O. U.	None	Diabetes mellitus	2¾
19	50	W	F	15	Myopia, senile cataracts	None	Hypothyroidism	3¼
20	48	N	F	2	None	Yes, L. E.	Hypertension	¾
21	47	N	F	3	Anterior synechiae	Yes, O. U.	Diabetes mellitus	3
22	46	N	M	3	Iris cysts	Yes, O. U.	None	2
23	48	N	M	4	Nuclear sclerosis, O. U.	Yes, O. U.	None	2¼
24	30	N	F	7	None	Yes, R. E.	None	1¼

* Simple glaucoma O. U. except where marked with double dagger (‡), indicating secondary glaucoma.
† Aside from glaucomatous optic atrophy.

Hereditary Optic Atrophy

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Congenital hereditary optic atrophy is a rare but important specific entity, which is seldom recognized by most ophthalmologists. It is distinct from Leber's hereditary optic atrophy, particularly as to its age of onset, course, relative absence of associated physical abnormalities, and pattern of hereditary transmission. In the majority of the cases described in the literature there is moderate pallor of both optic discs with sufficient atrophy so that the cribiform plates are well made out. There is moderate to severe loss of vision. Physical abnormalities, other than optic atrophy, are not found consistently in affected persons. The optic atrophy is thought to be present at birth. Hereditary optic atrophy affects both sexes, and it may be transmitted in a dominant manner to successive generations through either the male or the female.

This type of congenital optic atrophy has been described in the literature by Gunn,[1] Griscom,[2] Thompson and Cashell,[3] Duke-Elder,[4] Scott,[5] and Loberg and Lund.[6] Duke-Elder[4] feels that these cases probably cannot be accepted as Leber's disease. Loberg and Lund[6] emphasize the fact that this disease is an important nosologic entity, with which ophthalmologists should become familiar.

Pedigree and Report of Cases

A young boy and a young girl were brought under observation because of poor vision. The family history of these two children, who were siblings, indicated further visual difficulties in the family. The members of the family were brought under observation, as far as this was possible. Five persons showing moderately severe optic atrophy were found in four generations consisting of eighteen persons. Another person, now deceased, can be presumed to have had the same condition. A further case shows a mild affection of the optic discs. Fourteen of the eighteen members of the family presented in Figure 1 came under examination at this time. The family is of mixed European extraction, and all members reside on the west coast of the United States.

CASE I_1.—The man of the first generation has been dead for a number of years, but, according to his refractionist, he always had suffered from grossly impaired vision, even with corrective lenses. It was believed that he suffered from the same affection which is present in his three living sons. He married a daughter (Case I_2) of his own cousin, and all members of the second generation, as shown in Figure 1, are from this union. Case I_2, who has remarried, was examined. She was found to have opacities in both corneas from on old inflammatory condition. She also showed advanced bilateral cataracts, and the optic discs could not be visualized. Although her vision is now seriously impaired, she did have very good vision in each eye at an earlier period of her life, and it is assumed that she is unaffected by optic atrophy.

CASE II_2.—A 42-year-old man, a son of Case I_1, has had poor vision since birth. With myopic lenses of moderate strength, vision of 20/50 in the right eye and 20/200 in the left eye was obtained. The pupils were equal and reacted to light stimulation and in accomodation. The media in each eye were clear. The optic discs were pale and there was a moderate amount of optic atrophy of each disc. The margins of the optic nerve heads were well defined. The

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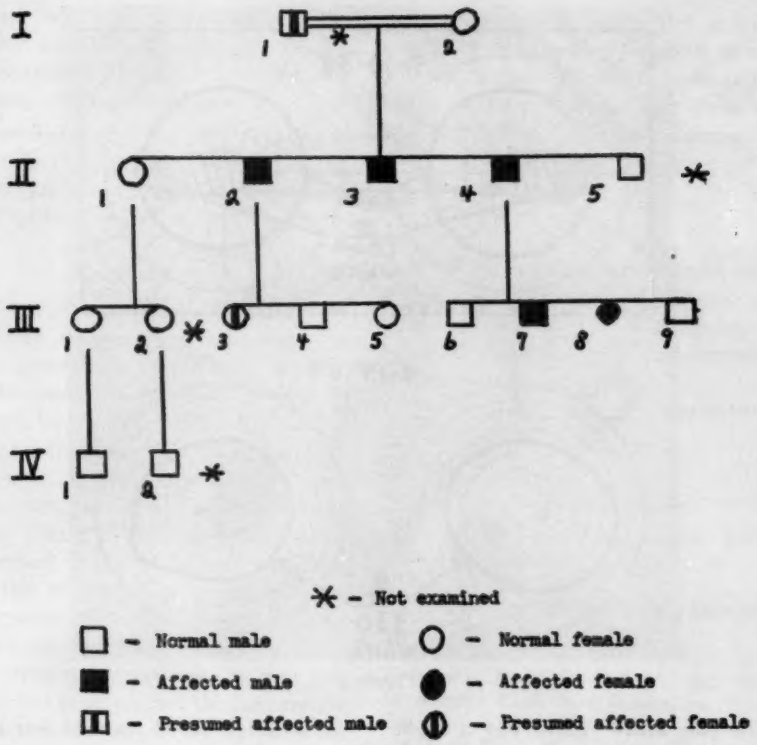

Figure 1

retinal vessels were not unusual, and the fundi were essentially negative in appearance.

CASE II_3.—A 39-year-old man, also a son of Case I_1, has had poor vision since birth. As far as he knows, there has been no change in his vision during his lifetime. His vision, with a small degree of hyperopic correction, was found to be 20/200 in the right eye and 10/200 in the left eye. There was a left esotropia of 40 degrees with eccentric fixation in the left eye. The intraocular tension measured 18 mm. Hg (Schiøtz) in each eye. Both of the optic discs showed moderate temporal pallor, with loss of substance and good visualization of the cribiform plates in the pale areas. There was no associated physical defect. The complete blood cell count, urinalysis, and repeated serological tests for syphilis over a period of many years revealed nothing abnormal. Visual field studies presented a scotoma of about 5 degrees surrounding the fixation area with the 1/1000 and 3/1000 white targets on the tangent screen. The field was full peripherally, with the 2/330 white target on the perimeter. Difficulty was encountered in studying the field of the left eye. There was no nystagmus.

CASE II_4.—A 37-year-old son of Case I_1 has had poor vision, without change, during his entire lifetime. With moderate myopic correction, the visual acuity for distance was 20/100 in the right eye and 20/200 in the left eye. The intraocular tension measured 20 mm. Hg (Schiøtz) in each eye. The pupils were equal, and they reacted promptly to light. There was no nystagmus or strabismus. Each optic disc showed moderate pallor and loss of substance temporally. The cribiform plates were easily made

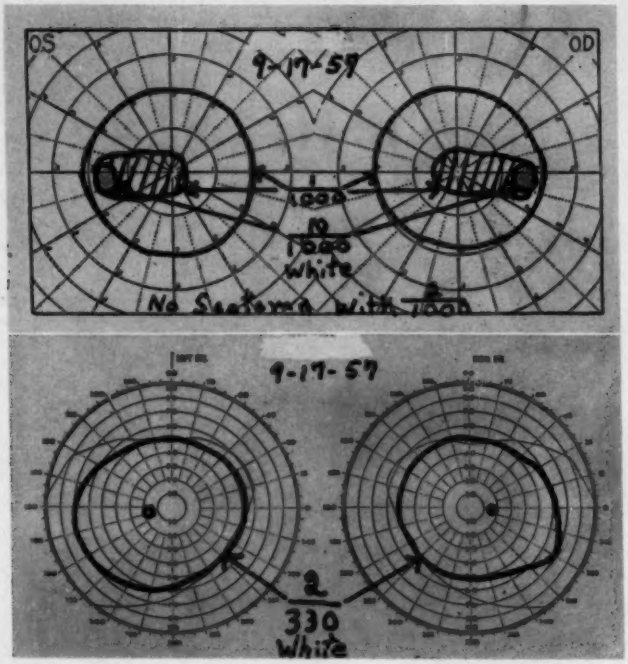

Figure 2

out in the pale areas. There was a slight pigment deposit in the macular area of each fundus. The retinal vessels were normal in appearance in both eyes. The general physical examination was otherwise normal. The complete blood cell count, urinalysis, and serologic tests for syphilis were negative. The visual field studies were charted on this patient and are shown in Figure 2. The peripheral fields were full. A relative cecocentral scotoma with the 1/1000 white target was found for each eye on the tangent screen examination.

Case III_3.—A 12-year-old daughter of Case II_2 has had good vision. Her vision could be corrected to 20/30 in each eye for distance with a moderate myopic correction before each eye. There was a definite pallor of a mild degree on the temporal portion of each optic disc. There was no nystagmus. The visual fields were not unusual. The ophthalmoscopic examination was otherwise normal bilaterally.

Case III_7.—An 8-year-old son of Case II_4 always has been known to have moderately impaired vision. With a small myopic correction before the eyes, his vision was improved to 20/80 in each eye. The pupils were equal, and they reacted promptly to light stimulation. The intraocular tension measured within normal limits for each eye with the tonometer. There was moderate pallor and loss of substance of the temporal portion of each optic disc. Each macular area showed mild stippling with pigment. This boy had cerebral palsy, with weakness of the muscles of the legs. Speaking was difficult, and there was some difficulty in postural balance. There was no nystagmus. There were 15 degrees of alternating intermittent exotropia.

Case III_8.—A 6-year-old daughter of Case II_4 always has had poor vision. With a small amount of myopic correction before each eye, she read 20/200 in each eye with the illiterate "E"-chart. The pupils were equal, and they reacted promptly to light

stimulation. Both optic discs showed moderate pallor and loss of substance of the temporal portions. There was no strabismus or nystagmus. Her general health was good.

Four members of the family, as indicated in Figure 1, were not examined. One of these was presumed to be affected, and three had no history of defective vision.

Comment

In this limited group showing hereditary optic atrophy, the trait was transmitted to successive generations by the male only but to either the male or the female. The family is too small, however, for this peculiarity to have any significance. The congenital optic atrophy was, apparently, inherited as a dominant trait in this family. Central scotomata with no peripheral contraction were observed in the visual field studies in two of the affected cases. As in other studies reported in the literature, there were present no consistently associated diseases. Consanguinity was present in the first generation of this pedigree, but this, apparently, exerted no influence. It is felt that the optic atrophy was present at birth in this study. Most authors seem to believe that the optic atrophy is congenital in nature. Scott,[5] however, feels that the atrophy comes on sometime after birth and up to the fourth year of life in the cases without nystagmus which he reports. This is a difficult question to solve, and it will take careful study of newborn infants in affected families to give the answer to this. Loberg and Lund[6] concluded from their studies that within the group of dominant optic atrophy both congenital and acquired forms are present.

Summary

A family showing five definite cases of hereditary optic atrophy in four generations is presented. The condition appears to be congenital, and it is transmitted as a dominant trait.

Dr. Harold F. Falls made suggestions in the preparation of this article.

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Uveitis Caused by Helminths and Protozoa

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Introduction

It has been recognized for many years in Africa and in certain areas of Central and South America that microfilariae of Onchocerca volvulus produce blindness (O'Connor and Hulse, 1932; Hissette, 1938, and Clark, 1947). Insect larvae have frequently been found to cause ocular myiasis (Anderson, 1935), and patients with African sleeping sickness have been reported to experience keratitis, iridocyclitis, and choroiditis (Ridley, 1945).

However, additional significant reports involving the relationship of other animal parasitic infections to uveitis have been presented within the last few years and require our attention.

(1) Helminths
- (*a*) Microfilariae other than those of Onchocerca: choroidal degeneration associated with microfilaraemia of Wuchereria, reported by Crawford et al. (1954)
- (*b*) Migratory larvae of Nematoda, reported by Wilder (1950), Nichols (1956), and Beaver (1956)

(2) Protozoa
- (*a*) Toxoplasma gondii as a cause of chorioretinitis, reported by Wilder (1952)
- (*b*) Central serous choroidosis associated with amebiasis, reported by Braley and Hamilton (1957)

Ocular infection with any living agent of disease, whether virus, bacterium, fungus, or animal parasite, should be looked upon merely as an incident during the general infection of man by that parasite. The life cycle of the parasite in man must be understood and the method of migration or transmission to the eye must be determined to appreciate the nature of these incidents.

If one is interested in pathology or therapy, the mechanism of infection must be sought, and if one is interested in prevention then the reservoirs, vectors, and routes of infection must be established. It is the purpose of this paper to summarize briefly the earlier knowledge of the topic under discussion and to review the more recent reports.

Review

1. *Helminthic Infections.*—Although involvement of the periorbital tissue by sparganum of Diphyllobothrium sp., of the orbit by the larval stage of Echinococcus, and of the posterior chamber by Cysticercus cellulosae are reported, Platyhelminthes has not been found in the uveal tract (Craig and Faust, 1951). However, Badir (1946) has reported Schistosoma haematobium adults from the superior ophthalmic vein of man. As cerebral schistosomiasis is known to occur in man, anatomically it would appear to be possible for eggs of Schistosoma to gain access to the eye through the circulation.

Members of the phylum Nematoda, however, are encountered in the eye more often. Adult Dirofilaria of several species have been reported from both the orbit and the cornea (Faust, 1957); Thelazia californiensis has been recovered from the conjunctival sac in California (Horsford et al., 1942) and the migration of adult Loa loa across the cornea occurs frequently in Africa. Sen and Ghose (1945) reported the recovery of Gnathostoma from a pigmented nodule on the iris of an eye in Calcutta. Apart from Gnathostoma, how-

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ever, involvement of the uveal tract by helminths appears to be limited either to microfilariae or to more mature larvae of Namatoda.

(a) Onchocerciasis: In onchocerciasis the microfilariae, which are found widely distributed through the dermis and connective tissue, gain access to the eye by direct migration to the aqueous humor and subsequently to the choroid and retina.

Adult worms have matured previously in skin tumors, usually located in subcutaneous or connective tissue nodules which may be located in varied areas of the body. In Africa most nodules occur on the trunk and limbs, while in Guatemala and Mexico they are found more frequently on the scalp. Although once reported, it has not been confirmed that adult Onchocerca occurs in the eyes.

The unsheathed microfilariae range from 150μ to 350μ in length and from 5μ to 9μ in diameter. They are extremely active and may migrate widely throughout the skin. An inflammatory reaction may accompany their presence and is thought to be allergic in character, probably brought on by the death of microfilariae and the liberation of antigenic materials from them. Once in the eye the microfilariae may find escape difficult, and death ensues. The reaction, according to Hissette (1938), produces a choroiditis often extending to chorioretinitis and producing blindness because the choroidal retinal lesions result in dystrophy of the optic nerve and later in atrophy. Death of the microfilariae may also be provoked by administering microfilaricides, e. g., diethylcarbamazine. The allergic reaction may also be prevented by giving cortisone (Markell and Turner, 1957).

Recommendations for prevention are (1) control of the insect vector, Simulium; (2) mass surgical removal of the nodules which contain adults, and (3) mass treatment with the microfilaricide diethylcarbamazine.

(*b*) Wuchereria bancrofti: Crawford et al. (1954) in Truk and adjacent islands of the Pacific have encountered a condition of choroidal degeneration. They cite a report by Leber (1914), who described a similar condition in Samoa, which he called retinosis and which he thought was caused by the microfilariae of W. bancrofti. In Crawford's opinion, only choroidal involvement occurs. It must be remembered that in Bancroftian filariasis, the microfilariae, in contrast to the situation in onchocerciasis, circulate freely in the blood stream. They measure from 2.5μ to 10μ in diameter and may readily pass into the capillaries of the eye. If this condition reported by Crawford is a common result of infection with W. bancrofti, it would seem that clinicians in areas where microfilaraemia is prevalent would have observed an increase in such choroidal degeneration in those same geographical regions.

Such has not been the case, and, to observe the possibility further, Dr. Herman Iverson, while on a recent trip to the Society Islands, checked 100 persons under study for filariasis at the Institut de recherches médicales de l'oceanie française with high microfilarial counts, i. e., above 100 per 20 cu. mm. A type of macular degeneration was observed in 12 eyes, but he found no destructive eye lesions similar to those described by Leber. He makes the following recommendations for study: "It is possible that filariasis does cause a choroidal lesion. It will be most difficult to prove this point. Several hundred cases, preferably observed in a dark room with full dilatation, should be checked. To rule out other causes of choroiditis will be difficult. Syphilis, tuberculosis, and toxoplasmosis will add diagnostic difficulties. Adequate controls should be available for a complete study. It would be of interest to check the ocular condition of filariasis further. It would also be of interest to check some of the other ocular conditions present in The Islands such as cataract and strabismus" (Iverson and Kessel, 1954, unpublished manuscript).

(*c*) Migrating Larvae of Nematoda: The migratory habits of the larvae of nematodes in man have long been an intriguing study to parasitologists. In hookworm infection and strongyloidiasis, filariform larvae usually enter through the skin; in ascariasis the second-stage larvae are usually liberated from the egg in the small intestine, and in trichinosis they are deposited by the adult female into the intestine. In all instances they reach the right heart by the venous circulation and are then carried to the lungs. From the lungs three main types of migration occur, dependent mainly on the size of the organisms. Microfilariae and Trichinella larvae, being less than 10μ in diameter, pass pulmonary capillaries unimpeded. Ascaris lumbricoides, Strongyloides, and human hookworm larvae, being more than 20μ in diameter, break through the alveolar spaces of the lungs, are coughed up, and reach their destination in the intestine through the trachea. According to Sprent (1955), larvae less than 20μ in diameter may undergo a somatic migration to many regions of the body.

Two diseases of man, "creeping eruption," or cutaneous larva migrans, and visceral larva migrans, are caused by larvae of worms, the adult stages of which normally mature in other animals. The former is usually caused by larvae of the dog hookworm, Ancylostoma caninum, or of A. braziliense, and visceral larva migrans, described by Beaver et al. (1952), to date has been shown usually to be caused by dog or cat ascarids of the genus Toxocara. This is primarily a disease of young children who often show association with puppies and in some instances give a history of eating dirt. A marked eosinophilia ranging from 20% to 80% and a high leucocytosis (cell count from 15,000 to 80,000) are characteristic. Tropical eosinophilia, eosinophilic pseudoleukemia, Weingarten's disease, and Loeffler's syndrome have frequently been used to describe similar or identical conditions with allergic characteristics. It is widely reported within the U. S., has been found in Puerto Rico and England, and probably occurs in widely distributed parts of the tropics.

Wilder (1950), in a meticulous study of 46 eyes from the Armed Forces Institute of Pathology on which the diagnosis of endophthalmitis had been made, reported the presence of nematode larvae in 24. Although Chitwood considered these to be third-stage hookworm larvae, it is of significance in the light of the above discussion on visceral larva migrans to note that all 24 eyes were from children, the majority being of preschool and early school age.

Nichols (1956) describes the differences between the second- and third-stage larvae of Toxocara canis, Toxocara cati, A. lumbricoides, Necator americanus, A. caninum, and Strongyloides stercoralis and furnishes a key, excellent drawings, and photomicrographs by which they may be differentiated. He and Beaver (1956) point out that the behavior of T. canis and of A. caninum larvae in the rodent host is similar and that both may be capable of producing visceral larva migrans in man. He has reidentified the nematode larvae from at least three of the eyes in Wilder's series as T. canis.

Recently also (1956) an eye was found by Dr. A. Ray Irvine Jr. in a child 3 years of age in which a nematode larva was present. The pathology encountered is compatible with that found by Wilder (1950). Beaver and Nichols (personal communication) have identified this larva as T. canis.

From these reports it would appear that not infrequently one may find invasion of the eye during or following either an acute or a subclinical attack of visceral larva migrans, or possibly of cutaneous larva migrans. If the report of Calhoun (1937) that active ascarid larvae may be observed in the eye is correct, this condition may be commoner than we imagine.

Prevention of infection with A. caninum or A. braziliense rests in wearing shoes and not coming in contact with soil where filariform larvae are active. Ingestion of food containing infective stages of T. canis or

T. cati will lead to infection by these species. Dogs and cats, especially those around children, should be given periodic checks for helminthic infections and treated appropriately.

The use of diethylcarbamazine has been proposed for cutaneous larva migrans and in conjunction with cortisone might also prove beneficial in visceral larva migrans. Heiner and Kevy (1956) suggest symptomatic treatment with corticosteroids or corticotropin (ACTH), and Dent et al. (1956) used cortisone in one case with benefit.

2. *Protozoa.*—(*a*) Trypanosomiasis: Reports on experimental trypanosomiasis in animals show that inflammation of the eye, caused directly by trypanosome infection, at times resembling interstitial keratitis of man, may occur. Although early literature on human trypanosomiasis indicated a number of eye conditions, e. g., keratitis and choroiditis, recent studies by Ridley (1945) indicate that many of these reports did not separate other tropical diseases, e. g., onchocerciasis, from their series. When complications from such diseases are separated, little severe ocular involvement is attributed to trypanosomiasis. In a series of 215 persons with uncomplicated trypanosomiasis, only 1 with interstitial keratitis, similar to that encountered in dogs infected experimentally with Trypanosoma gambiense, was encountered. No cases of choroiditis were observed. Ridley concludes that intraocular trypanosome infection cannot be regarded as a common or important cause of impaired sight in Africa.

Although edema around the eyes and conjunctivitis may accompany an early attack of Chagas' disease, or American trypanosomiasis, no evidence has been presented to indicate that uveitis results from the presence of Trypanosoma cruzi in the blood stream.

(*b*) Toxoplasmosis: T. gondii as an etiologic agent of uveitis is recognized both in congenital and in postnatal toxoplasmosis (Wolf et al., 1939; Wilder, 1952, and Jacobs et al., 1954). This part of my paper will be brief and limited to several nonclinical aspects of this fascinating topic.

(1) Phylogenetic relationships. It has been proposed to classify T. gondii either among the Mastigophora or the Sporozoa in the phylum Protozoa. Toxoplasma organisms have not been shown to possess flagella or blepharoplasts, but grossly they do resemble the spores of certain Sporozoa. The "pseudocysts" likewise are suggestive of this relationship. Recent morphologic studies by Gustafson et al. (1954) and Goldman et al. (1957) show structures, designated as "conoid" and "toxoneme," which are unique to these organisms. Their method of mitosis and cell division is likewise individualistic. From the point of view of host-parasite relationship, they have a broad range both in the animals and in the cells parasitized. Such relationships among the Sporozoa are usually highly specific. For these reasons, it appears that one should reserve judgment concerning their classification until more is known with reference to their taxonomic relationships with other organisms.

(2) Culture. Being intracellular in habitat, it is not surprising that Toxoplasma can be propagated only in animals or in tissue culture. The albino mouse is the most satisfactory means of cultivation known at present. However, toxoplasmas so grown, when used for antigens in laboratory tests and experiments, are subject to complex and nonspecific problems. For this reason there is a trend toward growing them in tissue culture. Guimaraes and Meyer (1942) and Jacobs et al. (1952) report growth with chick embryonic tissue. Chernin and Weller (1954) used roller-tube cultures and later HeLa cells. Vischer and Suter (1954) used cultures of macrophages from rodents. Eichenwald (1956) appears to have had success with several procedures in preparation of antigen, and it is anticipated that tissue-culture antigen will become increasingly practical in routine laboratory use.

(3) Epidemiology. Following the discovery of T. gondii by Nicolle and Manceaux (1908), it has been found as a natural parasite in a wide range of wild and domestic animals (Jacobs, 1956; Beattie, 1957; Feldman and Miller, 1956; Gronroos, 1956; Cathie, 1957, and Gibson and Eyles, 1956). Likewise, the dye test has been positive in a broad series of animal surveys and is stimulating additional studies. Surveys on human serums from many parts of the world have also been reported, probably most recently summarized by Feldman and Miller (1956).

These findings have led to the working hypothesis that a variety of animals may serve as reservoir hosts and that man is subject to subclinical or latent infections only occasionally giving rise to a frank expression of the disease or clinical manifestations. The rare uveitis falls into this category, usually being recognized only a considerable period of time after the generalized infection.

As a result of this hypothesis, much speculation and a number of experimental studies have been carried on with reference to the transmission of the organism. Because of the variety of animals involved and the multiplicity of tissues invaded, multiple modes of transmission, even including the possibility of an arthropod vector, would appear to be a highly inviting theory. However, until more exacting experiments are performed and confirmed from a greater variety of approaches, the more conservative attitude of the agnostic is preferred.

(*c*) Amebiasis: Braley and Hamilton (1957) reported nine persons with macular lesions or central serous choroidosis, all of whom showed signs of clinical amebiasis. Entamoeba histolytica was recovered from the stools of six of these patients, and serum from the other three yielded positive complement-fixation tests for E. histolytica. Coincidentally with accepted treatments for amebiasis both the intestinal symptoms and the macular lesions improved. The eye lesions healed, and vision improved or remained stationary.

The authors suggest that the lesions in the eye may represent direct invasion of the tissues by the parasite or that the lesion in the retina may represent a degree of hypersensitization in the absence of the amebae.

The close correlation of the eye lesion, as described, with intestinal amebiasis and positive laboratory results, plus the fact that both the intestinal lesions and the eye lesions improved under standard amebic therapy are indeed provocative to future investigation. Twice in my experience in tropical areas, I have met physicians, one an ophthalmologist, who routinely required stool examinations for E. histolytica in patients where eye conditions suggested allergic signs. The ophthalmologist believed that chronic amebiasis frequently predisposed to sensitivity states of the eye.

The conservative attitude and thorough procedures of diagnosis, treatment, and follow-up employed by Drs. Braley and Hamilton indicate that they are thoroughly cognizant of the problems involved in proving that a new clinical condition is in reality a type of systemic amebiasis. Theoretically, systemic amebiasis as secondary to intestinal involvement is possible and may exist as an amebic abscess or hepatitis, at times extending to the lung or brain. On occasion cutaneous amebiasis exists, and other rare secondary lesions have been reported. Searching for and finding E. histolytica in remote tissues of the body is no easy task, and this, coupled with the problem of procuring a suitable eye for examination in the first place, will make the task doubly difficult.

The complement-fixation test for amebiasis has recently fallen into a doubtful status, although I am one to believe in its value and hope that a stable antigen can soon be prepared. Other serologic tests should be studied to aid in the routine diagnosis not only of chronic amebiasis but also of the eye condition here reviewed.

In summary, it appears that Drs. Braley and Hamilton may have found a new and valuable treatment for the type of macular lesions in the eye which they describe. They have also added another possible etiologic agent to a field that already is complex, and they have provided the ophthalmologist and laboratory worker with another intricate problem of diagnosis.

Summary

Both helminths and protozoa have been found in the uveal tract in man.

The helminths are all developmental forms and are represented by (*a*) microfilariae of Onchocerca and possibly Wuchereria and (*b*) migrating larvae of other Nematoda. The latter most probably occur as an incident to visceral larva migrans, which is caused most frequently by Toxocara canis.

Protozoa reported to be etiologic agents of choroidal injury are the following: (*a*) Trypanosoma. More recent studies, however, indicate that trypanosomiasis alone is rarely associated with keratitis or choroiditis. (*b*) Toxoplasma gondii, which has been definitely shown to be responsible for chorioretinitis of man. This may occur in toxoplasmosis either of the congenital or of the postnatal type. (*c*) Entamoeba histolytica. Certain cases of central serous choroidosis occurring in association with amebiasis have been found to respond to standard amebic therapy. Either a direct invasion by E. histolytica into the tissues or a hypersensitization in the absence of amebae in the macular lesion is suggested.

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Observations on the Methylene Blue Dye Test for Toxoplasma

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Introduction

Toxoplasma gondii was discovered by Nicolle and Manceaux (1908) in a rodent from northern Africa, and the first authentic human infection was documented 29 years later, reported by Wolf et al. (1937). It has been only during the last few years that the disease in man has attained clinical importance. Toxoplasmosis exists in two main forms: (1) Congenital toxoplasmosis is that in which the infection passes through the placenta from an asymptomatic mother to her infant. This form of the disease occurs as encephalitis and may be accompanied by chorioretinitis, hydrocephalus, microcephaly, microphthalmus, intracerebral calcification, or mental retardation. (2) Postnatal toxoplasmosis is acquired either in childhood or adult life, probably from a closely associated animal reservoir, and may present symptoms of remittent fever together with pneumonitis, encephalitis, myocarditis, or myositis often accompanied by a mild generalized lymphadenopathy. A maculopapular erythematous rash may be present. In the past this second form of the disease often must have been passed by as a fever of unknown origin.

The chorioretinitis accompanying the congenital form led to the suspicion that T. gondii was the etiologic agent of certain undiagnosed types of uveitis which followed postnatal or acquired toxoplasmosis. The brilliant studies of Wilder (1952) on a series of enucleated eyes collected at the Armed Forces Institute of Pathology and the subsequent isolation by Jacobs et al. (1954) of T. gondii from an eye recently enucleated place toxoplasmal uveitis, as one expression of the disease, in an important and dramatic position.

It is readily seen that a reliable and safe method of laboratory diagnosis is much to be desired in order to differentiate actual toxoplasmosis from other suspected clinical entities.

The organism T. gondii is tentatively classified as a protozoon. It lives as an intracellular parasite and stimulates the production of antibodies. Although such antibodies are not always of practical application in the laboratory diagnosis of diseases caused by animal parasites, their use in toxoplasmosis appears to be satisfactory.

To date several serologic tests have been suggested for use.

(1) *The Neutralization Test.*—This procedure, as developed for virus diseases, was the first test applied, but never became highly popular because it was an expensive and cumbersome test to perform.

(2) *Methylene Blue Dye Test.*—Sabin and Feldman (1948) developed the methylene blue dye test. This, as now used at the National Institutes of Health by Jacobs, has been applied in the current study. Although the methylene blue dye test is complex and the personal factor in its application may account for reported variables in the hands of different workers, it is at

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present the most widely used of any of the laboratory procedures.

(3) *Hemagglutination Test.*—The agglutinogen is prepared by adsorbing Toxoplasma antigen to red cells. In this category, Jacobs and Lunde (1957) have described "A Hemagglutination Test for Toxoplasmosis." The authors employ a distilled water extract of organisms which is adsorbed to tanned fresh sheep cells. In application of the test, all serums must be adsorbed with sheep cells to remove antisheep antibody. The amount of antigen put onto cells and also its purity will influence sensitivity. McKenna (1957) has recently reported that formalin-fixed cells subsequently treated with tannic acid and to which bovine serum albumin or bovine γ-globulin were adsorbed remained stable for several months. Other workers using various antigen-antibody systems have reported that tanned human O-negative cells may be utilized instead of sheep cells. The use of tanned red blood cells is an easy procedure to learn and requires very little technician's time if a stable antigen cell suspension can be prepared. Results to date are variable and require confirmation. Coudert and Coly (1956) have adsorbed antigen to collodion particles instead of red blood cells. Sensitivity attained in the adsorbtion test is not as great as that procured in the dye test.

(4) *Complement-Fixation Test.*—This test uses antigen collected from mouse peritoneal fluid; from eggs, that is, the chorioallantoic membrane, or from tissue culture. The antigen from eggs is considered highly specific after a high-speed centrifugation and is not anticomplementary. Antigen from mouse peritoneal fluid is potent, but anticomplementary problems may arise. With use of 2 units of complement, the test is considered to be specific. Complement-fixing antibody appears during the acute phase of toxoplasmosis infection but persists for a shorter period of time than the dye-test antibody.

(5) *Precipitin Test.*—O'Connor (1957) demonstrated a precipitin reaction, using concentrated high-titer rabbit immune globulin and antigen from mouse peritoneal fluid. This was performed both in tubes and in using the agar-diffusion method of Ouchterlony (1949). O'Connor later employed aqueous humor as a source of antibody and tested it against antigens from Toxoplasma, Histoplasma, Streptococcus, and Staphylococcus and with PPD, by the Ouchterlony technique. He demonstrated a precipitin of the Toxoplasma antigen and correlated his results with the dye test, using both the aqueous fluid and the patient's serum.

(6) *Fluorescein-Labeled Antibody.*—Goldman (1957) has recently reported on a test in which fluorescein-labeled anti-Toxoplasma globulin is utilized. The organisms are fixed to a slide, and the slides are stored, frozen at −20 C. The labeled globulin competes with the unknown test serum for reactive sites on the organism. After appropriate rinsing, the organisms are observed through an ultraviolet microscope; fluorescent organisms are seen if the test serum is negative. Nonfluorescent organisms indicate a positive test serum. According to Goldman's report, the test requires less technician's time than the dye test and gives similar results. However, because of the cost of the fluorescent microscope and a difficulty in procuring fluorescein-tagged globulin, the test has not been checked by other workers to date.

By one or another of these tests, the commonest, however, being the methylene blue dye test, epidemiologic surveys in many areas of the globe and tests on persons suspected of having clinical toxoplasmosis have been performed. These studies have led to the hypothesis that acquired toxoplasmosis is a widespread benign infection in man, only rarely producing recognizable clinical manifestations. See Feldman and Miller (1956), Gronroos (1955), and Beattie (1957) for recent summaries.

Certain workers, notably Muhlpfordt (1951), Hein (1952), Michalzik (1953), Kulasiri (1954), and Awad (1954) have reported cross reactions with the complement-fixation and the methylene blue dye tests which would cast some doubt on their specificity.

When I began studies on toxoplasmosis, it seemed desirable especially to repeat the work of Awad (1954), in which he reported the production of antibodies to T. gondii in rabbits and mice infected with Trichomonas vaginalis and Trypanosoma cruzi. The work now to be reported was done primarily for information in my own laboratory. However, the recent article by Cathie (1957) on the appraisal of serologic tests has stimulated me to report the findings in confirmation of the validity of the methylene blue dye test.

Experimental Work

1. *With T. Vaginalis.*—Kelly et al. (1954) established infections of T. vaginalis by inoculation of pure cultures in white mice by both the intraperitoneal and the intramuscular routes with the objective of testing their immunity to subsequent homologous infection.

(*a*) In Mice: With use of this method, groups of mice were given inoculations one week apart of three injections of 0.5 cc. suspensions of T. vaginalis grown in the cysteine-peptone-liver maltose medium of Johnson and Trussell (1943) by (1) the intraperitoneal route, containing 2,000,000 trichomonads per cubic centimeter, and (2) the intramuscular route, containing 1,000,000 trichomonads per cubic centimeter. Foci of infection in the mice were established by both routes, and active T. vaginalis was recovered six weeks after the last injection from 70% of the mice infected by the intraperitoneal route and from 50% of the mice given inoculations by the intramuscular route.

Nineteen mice previously given inoculations of T. vaginalis by this procedure were subsequently given inoculations of a light dose of the RH strain of T. gondii, i. e., one-twentieth of the standard dose used for injection of animals for harvesting antigen for the dye test. All mice died within nine days, thus exhibiting no immunity to toxoplasma.

The serums from 39 other mice previously given inoculations by the same methods were bled and pooled in lots of 9 or 10 each, and the pools were subsequently subjected to the methylene blue dye test. All pools were negative to this test.

The results are summarized in Table 1 and contrasted with those of Awad. It will be seen that all of Awad's animals developed antibodies to T. gondii, while none of the animals in the current experiment developed such antibodies.

(*b*) In Rabbits: Three series of experiments were performed with rabbits, as follows.

Series 1. The serums from six adult rabbits were each tested for antibodies of T. gondii by the methylene blue dye test and were negative. One rabbit was kept as a control, and five were given injections twice, intravenously, one week apart, of 1.5 cc. of pure living cultures of T. vaginalis containing 1,000,000 trichomonads per cubic centimeter. Three weeks after the last injection serum was collected from all six animals and again tested by the methylene blue dye test.

Series 2. The same procedure as in Series 1 was followed with three rabbits, except that the animals were injected with T. vaginalis antigen that had been inactivated by alternate freezing and thawing rapidly three times before injection.

Series 3. The same procedure as in Series 1 was followed with four rabbits.

TABLE 1.—*Mice Given Inoculations of T. Vaginalis; Serums Later Tested by Dye Test Against Toxoplasma Gondii*

	Controls			Experiment			
	No.	Pos.	Neg.	No.	Pos.	Neg.	Remarks
Awad	6	0	6	12	12	0	Titers from 128 to 512
Kessel	20	0	20	39	0	39	All negative

TABLE 2.—*Rabbits Given Inoculations of T. Vaginalis; Serums Later Tested by Dye Test Against Toxoplasma Gondii*

	Controls			Experiment			
	No.	Pos.	Neg.	No.	Pos.	Neg.	Remarks
Awad (Tested before experiment only)	3	0	3	3	3	0	Titer 512
Kessel							
Series 1	6	0	6	5	0	5	Trichomonas living
Series 2	3	0	3	2	0	2	Trichomonas dead
Series 3	1	1*	0	3	2*	1	Trichomonas living
(Tested before and after experiment)							
Total	10	1	9	10	2	8	

* Titer 1:8.

The results are shown in Table 2 in contrast to Awad's results.

It will be observed that all three of Awad's rabbits developed antibodies to high titers, as tested by the methylene blue dye test, while none of the rabbits in Series 1 and 2 developed such antibodies.

The results of Series 3 differed in that the control animal and two of the experimental animals during the experiment developed low dye test titers (1:8). Sera were inactivated before the test was performed.

2. With T. Cruzi.—T. cruzi employed in these infection experiments were collected from Triatoma protracta caught in nests of the wood rat, Neotoma, in Griffith Park, Los Angeles (Wood, 1940). The contents of the hind gut from bugs found to be positive were diluted with isotonic saline and injected subcutaneously or intramuscularly into young unweaned mice and rats. Blood collected from their tails, on or before the 17th day after inoculation, all showed typical "s" and "c" trypanosomes with large terminal basal granules characteristic of T. cruzi. The first six animals were bled and the serums were tested at six weeks. A second lot was bled and tested at 10 weeks.

TABLE 3.—*Mice or Rats Given Inoculations of T. Cruzi; Serums Later Tested by Dye Test Against T. Gondii*

	Controls			Experiment			
	No.	Pos.	Neg.	No.	Pos.	Neg.	Remarks & Titers
Mice							
Awad	4 From colony	0	4	4	4	0	1 at 256 3 at 512
Kessel							
Series 1 (6 wk.)	3	0	3	6	0	6	All negative
Series 2 (10 wk.)	3 Mothers of litters	0	3	6	0	6	All negative
Rats							
Kessel							
Series 1 (6 wk.)	3	0	3	6	0	6	All negative
Series 2 (10 wk.)	3 Mothers of litters	0	3	6	0	6	All negative

TABLE 4.—*Dye-Test and Toxoplasmin-Test Results in Persons with Uveitis*

Dye-Test Results	Skin-Test Results	No.	Jacobs' Series
Negative	Negative	66	86
Negative	Positive	3	23
Positive (1:1 or higher)	Positive	64	68
Positive (1:1 or higher)	Negative	34	16
Total		167	193

From Table 3 it will be noted that neither mice nor rats infected with T. cruzi in the current experiment developed dye-test antibodies to T. gondii.

Correlation of Methylene Blue Dye Test and Toxoplasmin Skin Test.—Serums from 167 persons with a clinical diagnosis of uveitis, forwarded to the Estelle Doheny Eye Foundation by interested ophthalmologists, were tested by both the methylene blue dye test and the toxoplasmin skin test.* The results are presented in Table 4 and discussed below.

Table 4 displays the total results in four combination groupings and in the last column lists a series from Jacobs et al. (1956) for comparison. It is of interest to note that the incidence of correlation where both tests agreed, i. e., the negative-negative group plus the positive-positive group, was 80% in both Jacobs' series and mine.

In Jacobs' series the incidence of correlation between the positive dye tests (at a

* The antigen for the toxoplasmin skin test was supplied by Eli Lilly and Company.

TABLE 5.—*Correlations of Skin-Test with Dye-Test Results*

Dye-Test Titers	No.	Skin-Test Positive	Skin-Test Negative	% Correlation
Negative	69	3	66	96
Positive	98	64	34	66
From 1:1 to 1:8	17	10	7	59
From 1:16 to 1:64	54	34	20	63
From 128 to 512	21	15	6	71
From 1024 & higher	6	5	1	87
Total	167	67	100	

titer of 1:64 or above) and the positive skin tests was 72%. My figure at this same level was 70%. At the lower levels, however, his incidence of correlation was higher than mine.

In Table 5 the results are arranged to show the incidence of correlation at six different levels.

It is observed from these results that (1) negative dye tests and negative toxoplasmin tests correlate to a high degree. A negative dye result would yield a negative skin test in 96% of those tested, thus indicating that a person negative by both tests would in all probability definitely be negative. (2) The per cent of correlation between positive dye tests and positive skin tests is, however, not so great. The incidence of correlation was 66% in the whole series. There is an ascending correlation from 59% to 87% in four groups listed in Table 5.

These results are presented at this time with the knowledge that they do not represent a complete picture. It is hoped that by comparison with other studies in which clinical and laboratory data are better correlated additional information will be provided, e. g., from the Laboratory and Clinic of the Proctor Eye Foundation, the 10th anniversary of which is being commemorated.

Comment

Recent reports by Frenkel (1956), Eichenwald (1956), Hogan (1956), Jacobs (1956), and Feldman (1956) indicate these authors to be satisfied that the serologic tests now in general use for toxoplasmosis are specific and trustworthy. Details of animal experiments designed to support this opinion are not presented, but Jacobs (1956) states that he has found no definite evidence that T. cruzi, Plasmodium berghei, Plasmodium gallinaceum, or Eimeria tenellum cross react serologically with T. gondii. Nor have Hepatozoon and Sarcocystis produced cross reaction in his laboratory. He does state, however, that in some instances rabbits infected with the closely related Besnoitia jellisoni show dye test titers up to 1:16.

Cathie (1957) discusses the cross reactions in low titers with the dye test between Sacrocystis and Toxoplasma reported by Awad and Lainson (1954) in sheep and considers that these are false-positive reactions resulting from some "toxoplasma-hostile factor" which disappears by heating at 56 C.

The report of Awad (1954) in which T. vaginalis and T. cruzi are so definitely stated to produce cross reactions with T. gondii would seem to require further investigation.

The current study was designed to determine whether antibodies to T. gondii could be developed in mice and rabbits by giving them inoculations of pure live cultures of T. vaginalis and whether mice and rats recovered from infections of T. cruzi possessed antibodies to T. gondii. The results as shown in Tables 1, 2, and 3 were consistently negative, with the exception of Series 3, where three rabbits, one control and two experimental animals, injected with T. vaginalis developed low dye-test titers during the experiment. Lainson (1957) reports the recovery of T. gondii from rabbits in which the infection was naturally acquired. Beverley et al. (1954) and Feldman (1956) further report that rabbits may possess naturally acquired dye-test antibodies to T. gondii. It is also known that rabbits may harbor Encephalitozoon, and Jacobs (1956) states that rats infected with Encephalitozoon may have a low dye-test titer. Whether antisera from the three positive rabbits listed in the current experiment possessed antibodies which developed in response to an infection of T. gondii or Encephalitozoon, naturally acquired during the experiment, or whether they possess the so-called Toxoplasma-hostile factor of Cathie might be questioned. It is less likely to be the latter, for the serums were inactivated before testing. In either event, this experiment does not nullify the dye test as a valuable tool in

laboratory work. It is of interest that Awad (1954) did not observe a separate control in his rabbit series during the course of his experiment.

It appears safe to conclude that all mice and rats in this study given inoculations of either T. vaginalis or T. cruzi failed to develop significant antibodies to T. gondii. Such data fail to support the hypothesis presented by Awad that high titer cross reactions with T. gondii occur in laboratory animals inoculated with T. vaginalis or T. cruzi.

Of additional interest is the fact that hyperimmune serum prepared in a rabbit to Entamoeba histolytica and serum from a guinea pig recovered from an infection with Trypanosoma equiperdum were likewise negative to the dye test.

Cathie (1957) has performed a series of dye tests on serums in England from both men and women harboring T. vaginalis and does not find a higher prevalence of positive results in either group than in the general population from the same area in England. He also procured 70 serums from persons in Africa who harbored Trypanosoma gambiense in their blood, and only 2 were positive for the dye test. Likewise, he procured 15 serums from Brazil from persons with Chagas' disease, and only 6, or 40%, were positive for the dye test in low titers. This percentage is not compared with a Toxoplasma survey from the same area, nor are the ages of the tested persons stated. He assumed, however, that this 40% is no higher than one would expect to find in the general population of the area.

All such negative findings as listed in this discussion involving protozoa which might questionably be related to T. gondii lend additional support to the opinion that infection of man or animals with these protozoa does not interfere with the specificity of the methylene blue dye test for T. gondii.

Even though this specificity of results in serologic tests for Toxoplasma appears to be certain, a genuine problem exists in the interpretation of these tests in relation to suspected clinical findings, e. g., uveitis. Jacobs et al. (1956) have made an analysis in Baltimore to evaluate this relationship and the comparison of dye and skin tests in this paper records a similar initial attempt from the Los Angeles area.

When there are so many suspected etiologic agents for uveitis, the clinican has a problem to determine which is the important one and, in a case of uveitis with a positive dye test and/or toxoplasmin test, whether the latter are of clinical or of merely epidemiologic significance. The closest cooperation between the clinician and laboratory workers is required in such evaluations.

Summary

Serologic tests proposed for the detection of antibodies of Toxoplasma gondii are summarized.

The question of the specificity of the methylene blue dye test is reviewed, and the results of its use in testing serums procured from mice and rabbits inoculated with pure cultures of Trichomonas vaginalis and from mice and rats recovered from infections with Trypanosoma cruzi are reported.

They were consistently negative at significant titers and support the opinion that the methylene blue dye test for T. gondii is specific.

A comparison of dye-test results with toxoplasmin skin test results shows a high correlation between tests which are dye-test negative. A smaller correlation occurs between positive dye tests and toxoplasmin tests.

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Sodium and Potassium Concentrations Following Acetazolamide

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The finding that acetazolamide, a potent carbonic anhydrase inhibitor, significantly decreases the aqueous flow rate [2-4,24] has led to the use of this drug as an investigative tool for the further study of the secretory mechanisms. Its mode of action in the eye is subject to controversy. Friedenwald [11] and Becker [1,5] favor a local action through the inhibition of carbonic anhydrase in the ciliary body, although other investigators do not subscribe to this view.[13,22,24,31] A study of the effects of the drug on the aqueous and plasma cation concentrations is necessary for a complete understanding of the drug action.

Method

Adult male albino rabbits weighing from 2.5 to 3.5 kg. were utilized, and each eye was used only once for aqueous puncture. They were allowed food (Wayne Rabbit Pellets) and water without restriction. Twenty-four hours before use they were transferred from the regular animal room to an air-conditioned laboratory, where all experimental procedures were ultimately carried out.

Acetazolamide was administered as a 10% solution of a sodium salt in distilled water. Rabbits received a single dose of 100 mg. per kilogram of body weight intraperitoneally. Isotonic saline was administered to rabbits intraperitoneally in a single dose of 1 ml. per kilogram of body weight.

All procedures were carried out on the restrained conscious animal, with use of topical tetracaine (Pontocaine) anesthesia. Blood samples were obtained with a heparinized syringe by cardiac puncture. All syringes were lightly coated with a silicone lubricant to minimize evaporation and carbon dioxide loss. The blood samples were immediately centrifuged anaerobically, and a plasma sample was then withdrawn into a second tuberculin syringe. All samples were weighed to an accuracy of 0.1 mg.

Sodium and potassium determinations were carried out on separate samples. In all cases, control blood and aqueous samples were intially withdrawn, with use of the right eye. After an interval of one day for the potassium experiments and four to five days for the sodium experiments, acetazolamide or saline was administered and a second set of blood and aqueous samples was subsequently removed with use of the left eye.

Sodium and potassium determinations were made with a standard flame photometer. The instrument error was determined by a comparison of the results from sample pairs of a standard solution in the normal range. For sodium, the mean absolute difference between members of each pair was 0.8% of the mean standard value for 12 pairs. For potassium, the mean difference was 1.1% of the standard value for an equal number of pairs.

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TABLE 1.—*Normal Aqueous and Plasma Concentrations in the Rabbit* *

Determination	Total No.	Aqueous, mM/Kg. Water	Plasma, mM/Kg. Water	Aq./Pl.
Sodium	60	147.0±1.00 (±7.77)	153.2±0.89 (±6.92)	0.959±0.005 (±0.042)
Potassium	94	5.41±0.069 (±0.671)	5.74±0.063 (±0.617)	0.948±0.018 (±0.105)

* Results expressed as mean ±S. E. M. (±S. D.).

Concentrations are expressed as millimoles (mM.) per kilogram of water, assuming a 7% solid content for plasma and a negligible content for aqueous. Statistical analysis included calculation of the standard deviation and standard error of the mean and use of Fisher's *t*-test for the determination of the significance between means.[7]

Results

The normal values of sodium and potassium concentrations in rabbit aqueous and plasma are presented in Table 1. The mean value for sodium and potassium are in agreement with values reported by other investigators.[8,10,17-19,23,24,26-28] The greater dispersion of the potassium values is consistent with wider range of normal potassium values reported in the literature.

The results in Table 2 demonstrate that the administration of saline was associated with a small but equal decrease in both aqueous and plasma potassium concentrations. This decrease was probably a result of the previous handling and cardiac puncture associated with the control sampling. The data in Table 3 illustrate that one-half hour after acetazolamide administration the decrease in aqueous and plasma potassium concentrations was significantly greater than that associated with saline injection. The decrease, however, was similar in the two fluids. The results in Tables 4 and 5 illustrate that a significant fall in concentrations was maintained for at least five hours and was equal in the two fluids. These findings are consistent with the results reported by other investigators for the rabbit [10,14,28] and for humans.[6,25]

The data in Tables 6 and 7 demonstrate that neither saline nor acetazolamide significantly altered the aqueous and plasma sodium concentrations two and one-half hours after administration. These results are consistent with those of Franceschetti et al.[10] and Langham and Lee [24] in the rabbit. They differ from the results of

TABLE 2.—*The Effect of Isotonic Saline on the Potassium Concentrations of Aqueous and Plasma* *

	Potassium Concentration, mM/Kg. Water		
	Control	Saline	Difference (Cont.—Sal.)
Aqueous	5.4±0.11 (±0.48)	5.0±0.14 (±0.56)	0.3±0.12 (±0.49)
Plasma	5.6±0.09 (±0.37)	5.3±0.10 (±0.41)	0.3±0.10 (±0.39)
Aq/Pl.		0.95±0.02 (±0.07)	

* Results expressed as mean of 16 determinations ±S. E. M. (±S. D.). Saline, 1 ml. per kilogram of body weight, given two and one-half hours before sampling. Aq. diff., $0.025 > P > 0.020$; Pl. diff., $0.010 > P > 0.005$; Aq. diff., to Pl. diff., $P > 0.90$.

TABLE 3.—*The Effect of Acetazolamide on the Potassium Concentrations of Aqueous and Plasma* *

	Potassium Concentration, mM/Kg. Water		
	Control	Acetazolamide	Difference (Cont. —Acetaz.)
Aqueous	5.3±0.11 (±0.50)	4.7±0.07 (±0.30)	0.6±0.08 (±0.34)
Plasma	5.5±0.12 (±0.52)	4.7±0.10 (±0.42)	0.8±0.11 (±0.50)
Aq/Pl.		1.00±0.02 (±0.09)	

* Results expressed as mean of 19 determinations ±S. E. M. (±S. D.). Acetazolamide, 100 mg. per kilogram of body weight, given intraperitoneally one-half hour before sampling. Aq. (acetazolamide diff. to saline diff.), $0.050 > P > 0.025$; Pl. (acetazolamide diff. to saline diff.), $0.005 > P > 0.001$; Aq. diff. to Pl. diff., $0.20 > P > 0.10$.

TABLE 4.—*The Effect of Acetazolamide on the Potassium Concentrations of Aqueous and Plasma*

	Potassium Concentration, mM/Kg. Water		
	Control	Acetazolamide	Difference (Cont. —Acetaz.)
Aqueous	5.4±0.10 (±0.48)	4.3±0.72 (±0.35)	+1.2±0.10 (±0.23)
Plasma	5.9±0.15 (±0.73)	4.8±0.10 (±0.46)	+1.2±0.18 (±0.89)
Aq/Pl.		0.91±0.03 (±0.10)	

* Results expressed as mean of 23 determinations ±S. E. M. (±S. D.). Acetazolamide, 100 mg. per kilogram of body weight, given intraperitoneally two and one-half hours before sampling. Aq. (acetazolamide diff. to saline diff.), $0.001 > P$; Pl. (acetazolamide diff. to saline diff.), $0.001 > P$; Aq. diff. to Pl. diff., $P > 0.90$.

TABLE 5.—*The Effect of Acetazolamide on the Potassium Concentrations of Aqueous and Plasma* *

	Potassium Concentration, mM/Kg. Water		
	Control	Acetazolamide	Difference (Cont. —Acetaz.)
Aqueous	5.4±0.10 (±0.46)	4.3±0.09 (±0.41)	+1.2±0.11 (±0.52)
Plasma	5.7±0.1 (±0.51)	4.6±0.12 (±0.57)	+1.1±0.14 (±0.64)
Aq/Pl.		0.94±0.03 (±0.12)	

* Results expressed as mean of 21 determinations ±S. E. M. (±S. D.). Acetazolamide, 100 mg. per kilogram of body weight, given five hours before sampling. Aq. (acetazolamide diff. to saline diff.), $0.001 > P$; Pl. (acetazolamide diff. to saline diff.), $0.001 > P$; Aq. diff. to Pl. diff., $0.60 > P > 0.50$.

Weinstein,[32] who observed a large decrease in the aqueous concentration of four dogs following acetazolamide. No associated plasma values were reported. In humans, Campbell et al.[6] reported a decrease in the plasma sodium concentration, while Nadell[25] observed no change in concentration. No change has been observed in the sodium concentrations of gastric[16] and cerebrospinal[29] secretions following their inhibition by acetazolamide.

The limitations of the present technique must be clearly kept in mind. For sodium, the standard error of the difference of the means in these statistical comparisons is 1.3% of the normal sodium concentration. As a change in sodium concentration of this magnitude can be biologically significant, the absence of a statistically significant alteration does not exclude the possibility of a biologically significant alteration. For potassium, the standard error of the difference of the means is 3% of the normal potassium concentration.

TABLE 7.—*The Effect of Acetazolamide on the Sodium Concentrations of Aqueous and Plasma* *

	Sodium Concentration, mM/Kg. Water		
	Control	Acetazolamide	Difference (Cont. —Acetaz.)
Aqueous	147.0±1.4 (±8.0)	144.0±1.1 (±6.4)	+2.6±1.5 (±5.7)
Plasma	154.2±1.2 (±6.5)	150.7±1.2 (±6.8)	+3.5±6.4 (±1.1)
Aq/Pl.		0.954±0.005 (±0.026)	

* Results expressed as mean of 32 determinations ±S. E. M. (±S. D.). Acetazolamide, 100 mg. per kilogram of body weight, given intraperitoneally two and one-half hours before sampling. Aq. (acetazolamide diff. to saline diff.), $0.80 > P > 0.70$; Pl. (acetazolamide diff. to saline diff.), $0.80 > P > 0.70$; Aq. diff. to Pl. diff., $0.70 > P > 0.60$.

TABLE 6.—*The Effect of Isotonic Saline on the Sodium Concentrations of Aqueous and Plasma* *

	Sodium Concentration, mM/Kg. Water		
	Control	Saline	Difference (Cont.—Sal.)
Aqueous	148.0±1.6 (±7.6)	146.2±1.6 (±7.5)	+1.8±1.6 (±7.3)
Plasma	153.6±1.5 (±7.0)	150.7±1.6 (±7.2)	+2.9±1.6 (±7.3)
Aq/Pl.		0.964±0.008 (±0.036)	

* Results expressed as mean of 21 to 22 determinations ±S. E. M. (±S. D.). Saline, 1 ml. per kilogram of body weight, given intraperitoneally two and one-half hours before sampling. Aq. diff., $0.30 > P > 0.25$; Pl. diff., $0.10 > P > 0.05$; Aq. diff. to Pl. diff., $0.70 > P > 0.60$.

Comment

As the alterations in aqueous potassium concentration can be explained by the associated plasma potassium alterations, the possibility of an active potassium transport across the blood-aqueous barrier is not supported by the results of the acetazolamide experiments. The presence of an aqueous excess of sodium in all species that have been studied[9] and the universality of sodium transport in the animal body[30] strongly suggest a primary active transport of sodium.

If the net transfer of water into the aqueous is secondary to the active transport of ions including sodium and if acetazolamide inhibits this active ion transport, a decrease in net transfer rate of water should be associated with a similar decrease in the active transport rate of sodium. Within the limitations of the present technique, the maintenance of the normal steady-state sodium concentration in the aqueous is consistent with this view. A decreased rate of net aqueous flow has been well documented by a variety of methods[5] and very probably indicates a decreased net transfer rate of water due to active transport. The turnover rate of radioactive sodium in the aqueous following administration of acetazolamide has been compared with the normal turnover rate in order to determine the alteration

in the active transport rate of sodium.[15,20] However, the expected decrease in rate was not observed. Analyses of the normal dynamics of radioactive sodium entry into the anterior chamber [12,21] strongly suggest that the technique is not sufficiently sensitive to detect alterations of sodium turnover rates resulting from alterations in the active transport rate of sodium. As Kinsey and Palm point out,[21] the shape of the accumulation curve of radioactive sodium in the anterior chamber is determined predominantly by the rate of sodium diffusion. As the error in these turnover studies has been estimated at approximately 20%,[11] the effect of a reduction in the active transport rate of sodium could easily escape detection.

Summary

The mean (± standard error of mean) normal values, obtained by flame photometry, for aqueous sodium and potassium concentrations in the rabbit are 147.0 (±1.00) and 5.41 (±0.69) mM. per kilogram of water. The associated plasma concentration values are 153.2 (±0.89) and 5.74 (±0.63) mM. per kilogram of water, while the aqueous-to-plasma ratios are 0.959 (±0.005) for sodium and 0.948 (±0.018) for potassium.

Acetazolamide produces a similar decrease in the potassium concentrations of aqueous and plasma for at least five hours after administration of the drug. No alteration of the sodium concentrations of the two fluids is obtained two and one-half hours after administration of the drug.

For sodium, the standard error of the difference of the means of the statistical comparisons is 1.3% of the normal sodium value. For potassium, the standard error of the difference of the means is 3% of the normal potassium value.

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Reactions of the Cellular Elements of the Corneal Stroma

A Report of Experimental Studies in the Rabbit Eye

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Up to the present time there seems to be some confusion about the nature, the origin, and the significance of the reactive forms of corneal cells under pathological conditions. The present paper represents an effort to demonstrate the main phases of the nonspecific cellular reactions of the cells of the corneal stroma. These reactions of the stroma cells will be compared with those of the cellular elements which invade the corneal stroma from the limbus. The cornea of the rabbit was chosen for this experimental study, since the histological slides of this tissue allow for a detailed photomicrographic recording of all its cells and their pathological changes. Furthermore, it is my impression that the reactions of the cells of the rabbit cornea are very similar to those in man.

Experimental Methods and Histological Technique

Corneae of normal rabbits were injured with (1) keratome incision, (2) keratome incision and bacterial infection, (3) scratching of the corneal epithelium and herpes-simplex virus, and (4) instillation and injection of colchicine (1% solution). The eyes were enucleated at different times following the different kinds of experimental trauma and were immediately fixed in bromformalin (Cajal solution). The corneae were then isolated, and flat sections of them were made on the freezing microtome. The "panoptic" silver carbonate method of del Rio Hortega[1] was used to stain these sections. All figures of this paper represent unretouched photomicrographs.

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Histological Findings and Comment

Different stages of nonspecific cellular reactions were found in the corneal stroma of all these corneae following the different kinds of trauma mentioned above. These reactions—and not the specific changes of the different pathological conditions—were observed and used for this study. The cellular reactions were composed of (1) reactions of the stroma cells (fixed cells of the corneal stroma), (2) findings in invading white blood corpuscles, (3) changes of invading fibroblasts, and (4) process of corneal vascularization.

The Reactions of the Stroma Cells.—The stroma cells of the rabbit cornea normally represent flat cells with one or two large round or kidney-shaped nuclei and many long straight processes (Fig. 1). These processes branch at about right angles and interconnect the stroma cells. Therefore, the cellular pattern of the normal stroma cells is that of a syncytium. The spaces between the corneal cells are filled by regular layers of corneal lamellae (the latter remained unstained by my technique).

Within an hour following the different kinds of corneal trauma distinct changes were found in the stroma cells of the involved corneal areas. A loss of the long straight processes was typical for these

Fig. 1.—Normal stroma cells of the rabbit cornea. Flat section, Hortega method, photomicrograph; × 700.

early reactive changes (Fig. 2). The stroma cells were then no longer interconnected; they were star-shaped and sometimes of a somewhat epithelioid form. Signs of degeneration were found in many of these cells. Hypertrophy and proliferation were not observed in this early stage.

It is not possible to give precise times following the trauma for all the further changes of the stroma cells and the invading cellular elements, since a certain phase of cellular reaction depends not only on the time after the trauma but also on its character and severity.

The early stage of stroma-cell reaction, with the destruction of the cellular processes and the loss of the syncytial pattern, very often represented only the first signs of irreversible damage. It was then seen to be followed by complete necrosis of the cells. Many stroma cells, however, were found to survive. The process of survival of the stroma cells found its histological expression in cellular hypertrophy and new formation of the processes (Fig. 3). The stroma cells in this phase still represented star-shaped elements with the same round or oval nuclei. A multitude of short

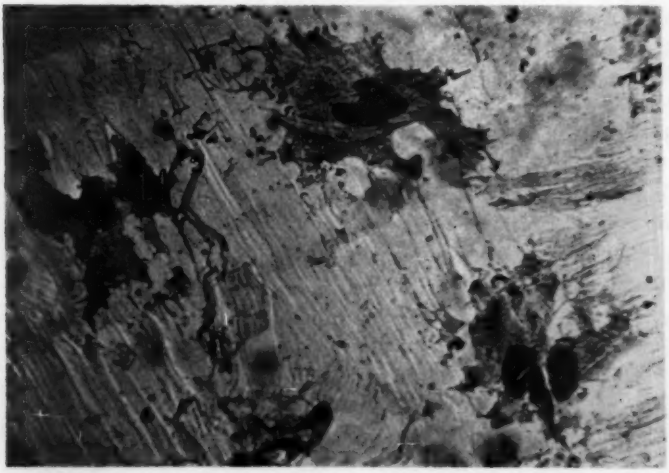

Fig. 2.—Early changes of stroma cells of the rabbit cornea. The cells are star-shaped and have lost their interconnections. Flat section, Hortega method, photomicrograph; × 700.

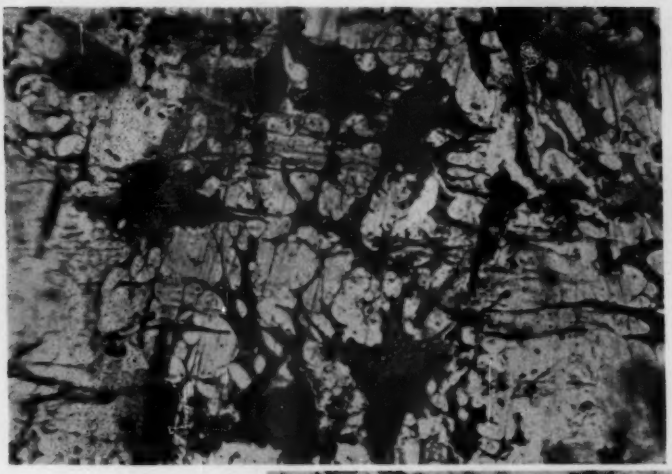

Fig. 3.—Stage of hypertrophy of stroma cells of the rabbit cornea. The new-formed cellular processes form a dense interconnected system. Flat section, Hortega method, photomicrograph; × 700.

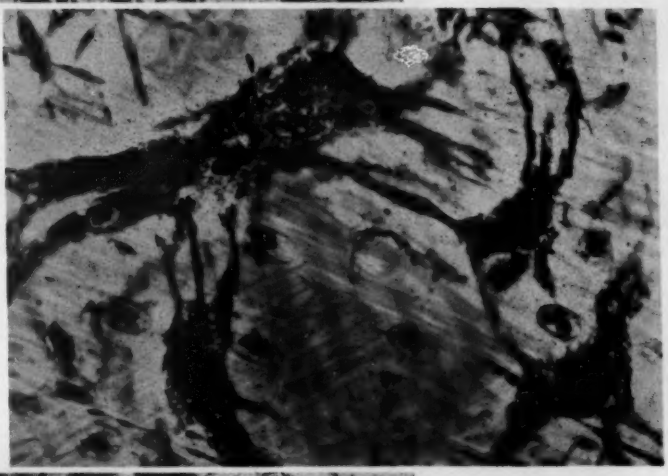

Fig. 4.—Stage of hypertrophy of stroma cells of the rabbit cornea. The cells also exhibit some degenerative changes and they are surrounded by leukocytes. Flat section, Hortega method, photomicrograph; × 700.

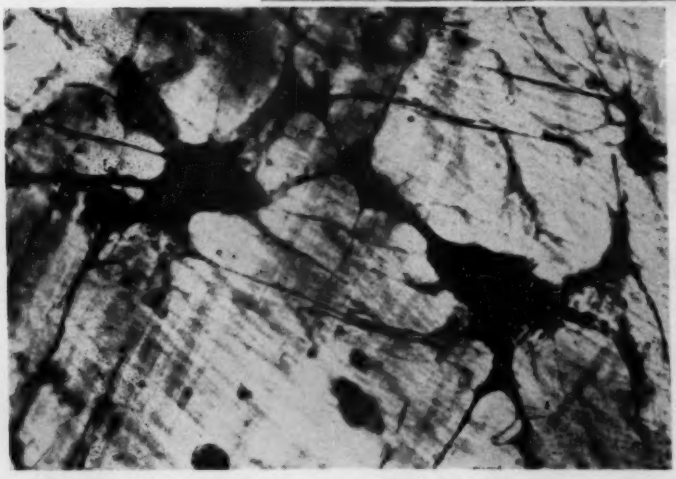

Fig. 5.—Very hypertrophic stroma cells of the rabbit cornea. Flat section, Hortega method, photomicrograph; × 700.

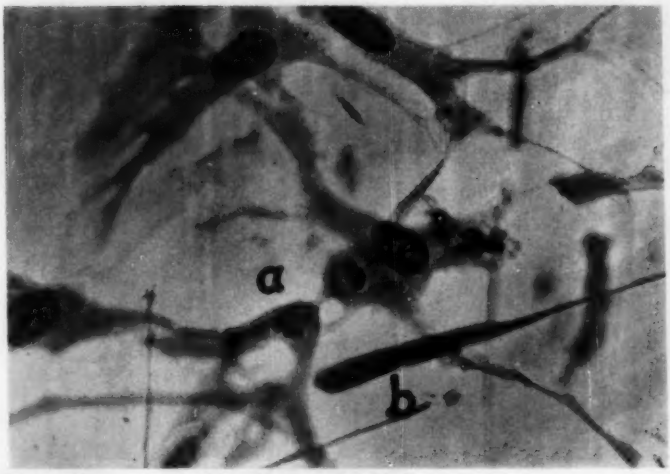

Fig. 6.—Stroma cells of the rabbit cornea in the stage of proliferation. There is cell division (*a*). A fibroblast is seen migrating between the stroma cells (*b*). Flat section, Hortega method, photomicrograph; × 700.

branched new-formed processes was seen around the cell bodies. These processes were again in contact with the processes of other hypertrophic stroma cells (Figs. 3 to 5). This phase of survival and cellular hypertrophy was somewhat different in different animals and after different types of trauma (Figs. 4 and 5). However, there always were the main characteristics of this stage: new formation of the lost processes and restoration of the syncytial pattern.

The next stage of stroma-cell reaction was that of cellular proliferation. Stroma cells were frequently found in different phases of cell division (Fig. 6). At the same time the stroma cells lost their delicate, branched processes and developed only few coarse processes (Figs. 6 and 7). These coarse processes were then observed to extend toward areas of the stroma, the cells of which had become necrotic in the early time after the trauma (Fig. 7). This process was very clearly visible in an area close to the cut of those corneae which had been injured with a keratome incision. There obviously was actual migration of proliferating stroma cells into such areas of the stroma which had suffered destruction of their stroma

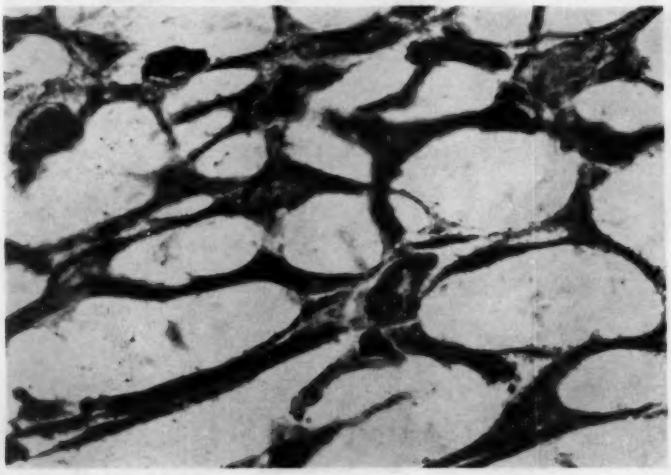

Fig. 7.—Phase of migration of proliferating stroma cells of the rabbit cornea. The cellular processes are very coarse. Flat section, Hortega method, photomicrograph; × 700.

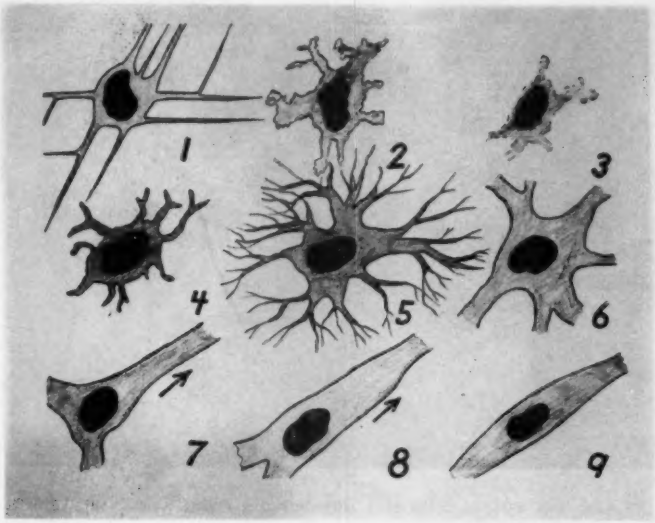

Fig. 8.—Drawing which demonstrates the changes of the corneal stroma cells of the rabbit as observed following experimental trauma. *1* represents the normal stroma cell; *2* and *3* show the early reactive and degenerative changes; *4* and *5* represent the stage of survival and hypertrophy, and *6* to *9* demonstrate the phase of proliferation and migration.

cells. These stroma cells then often represented rather simple, spindle-shaped cells. But they still had their large oval or kidney-shaped nuclei. In our silver-stained flat sections these migrating stroma cells were clearly distinguishable from invading fibroblasts (Fig. 13).

The Findings in Invading White Blood Corpuscles.—There is not very much to say about the invasion of the corneal stroma by leukocytes and lymphocytes which could be observed following the different kinds of corneal trauma. The nature, origin, and function of these cells is very well known in the literature. There certainly was no evidence in our cases that these cells ever develop from corneal stroma cells or epithelial cells, as recently suggested by Busse-Grawitz [2] and Pau.[3] It was obvious that all the white blood cells invaded the corneal stroma from the limbus.

It was very interesting to observe that immigrating leukocytes and lymphocytes were often found to wander in long straight chains through the stroma (Figs. 9 and 10). This fact was even more surprising since

Fig. 9.—A chain of lymphocytes which wander through the corneal stroma. Flat section, Hortega method, photomicrograph; × 500.

Fig. 10.—Another chain of lymphocytes which migrate toward the center of the corneal stroma of a rabbit. Stroma cells and single inflammatory cells are seen around it. Flat section, Hortega method, photomicrograph; × 500.

the direction of these chains did not correspond with the direction of the fibers of the surrounding corneal lamellae. The general direction of these chains of white blood cells in the cornea was usually approximately radial. It was my impression that these cells used some kind of a preformed space, and it seems very possible that these spaces represent the same structures which are known as Bowman's channels of the corneal stroma.[4] These channels have been demonstrated by air injection into the corneal stroma.[5,6]

In contrast to the chains and invading white blood cells, it was obvious that single cells and the dense accumulation of inflammatory cells in the stroma were always arranged according to the direction of the lamellar fibers (Fig. 11). Such a regular arrangement of these cells was only missing in more advanced stages of corneal inflammation, when the corneal lamellae were destroyed (corneal abscess).

The Changes of the Invading Fibroblasts.

Invading fibroblasts were found only in those corneae which showed severe involvement of the stroma. These fibroblasts represented long and mostly spindle-shaped cells with a small elongated nucleus (Figs. 12, 13, and 14). They were always distinctly

Fig. 11.—Dense inflammatory infiltration of the corneal stroma. The cells are arranged according to the direction of the fibers of the unstained corneal lamellae. Flat section, Hortega method, photomicrograph; × 500.

Fig. 12. — A hypertrophic stroma cell (*a*) and an invading fibroblast (*b*) of the corneal stroma of the rabbit. Flat section, Hortega method, photomicrograph; × 700.

Fig. 13. — Two typical immigrating fibroblasts of the stroma of the rabbit cornea. These cells have a very small and elongated cellular nucleus. Flat section, Hortega method, photomicrograph; × 700.

Fig. 14. — Numerous fibroblasts invading the corneal stroma of the rabbit. Flat section, Hortega method, photomicrograph; × 500.

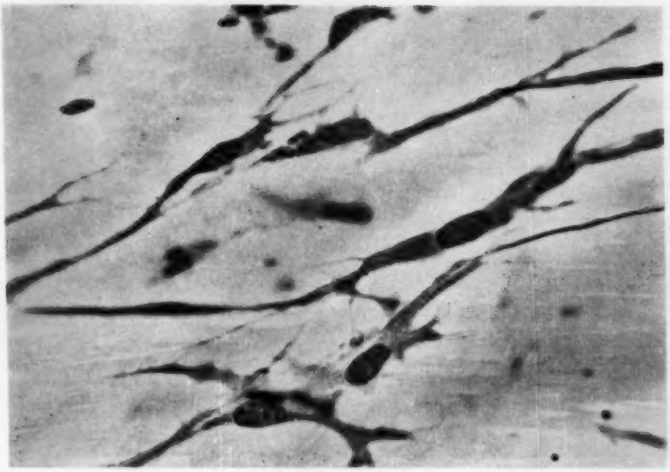

Fig. 15. — Fibroblasts in a healed scar of the corneal stroma of the rabbit. These cells have a somewhat stroma-cell-like appearance. But they still clearly represent fibroblasts. Flat section, Hortega method, photomicrograph; × 700.

different from stroma cells and could be distinguished from the proliferating, migrating forms of stroma cells. This morphological difference between invading fibroblasts and the reactive forms of stroma cells must be emphasized, since it has been said in the literature that irritated stroma cells may change into fibroblasts.[7] However, it was my impression that corneal stroma cells represent a special type of fibroblasts which could not be observed to lose their differentiation completely and which were not seen to change into nondifferentiated, wandering fibroblasts. On the other hand, it was also never seen that the invading fibroblasts became quite like corneal stroma cells. In the old scars following the experimental corneal injuries the fibroblasts had become somewhat stroma-cell-like (Fig. 15). They then had branched processes, but they still had the small elongated nucleus which is typical for fibroblasts. The shape and distribution of their processes also never quite resembled those of corneal stroma cells.

The Process of Corneal Vascularization.

In the cases of severe and more prolonged experimental keratitis there always

Fig. 16. — New-formed blood vessel of the corneal stroma of a rabbit which is filled with blood. The bud-like point of this vessel is composed of endothelial cells. Flat section, Hortega method, photomicrograph; × 500.

occurred vascularization of the corneal stroma. All stages of the new growth of blood vessels into the stroma from the limbus could be observed. Usually the limbus vessels formed bud-like formations of endothelial cells which extended into the stroma. These structures were at first solid and contained no blood. Later a lumen developed and was filled with erythrocytes (Fig. 16). These observations are in agreement with the classical understanding of corneal vascularization. But they are in contrast to the recent report of Pau,[8] who believes that the corneal blood vessels are formed by corneal stroma cells.

Comment.—As the more important results of this study we would like to emphasize the following: 1. The corneal stroma cells (fixed cells of the corneal stroma) are even in their reactive and migrating forms distinctly different from the invading fibroblasts. 2. The lymphocytes and leukocytes were found to immigrate from the limbus and were not seen to develop within the stroma from stroma cells. The observation of long straight chains of migrating leukocytes or lymphocytes was considered indirect evidence for the existence of the so-called corneal channels of Bowman. 3. The invading fibroblasts never seemed to become quite like stroma cells. However, in old healed scars after experimental keratitis they often appeared somewhat stroma-cell-like. 4. The blood vessels which invade the stroma in the process of corneal vascularization were formed by proliferation of endothelial cells of the blood vessels at the limbus and not by stroma cells.

Summary

The reactions of the cellular elements of the rabbit cornea following experimental trauma were studied and compared with the nature and changes of the cells which invade the stroma secondarily.

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Mandibulofacial Dysostosis (Franceschetti Syndrome)

A Case of the Complete Syndrome

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In 1944, the Franceschetti syndrome was recognized as a distinct clinical entity.[1] This was followed by the definitive work of Franceschetti and Klein in 1949.[2] As a rule, this developmental anomaly does not appear as the full syndrome and has been subdivided into five groups: 1. Complete. This form, which is composed of multiple congenital malformations of the face, mouth, eyes, and ears, was first described in 1923 by de Lima and Monteiro[3] but failed to appear in the American literature until the reports of Hurwitz,[4] in 1954, and Hunt and Smith,[5] in 1955. 2. Incomplete. Despite the usual report of deafness in this commoner form, the ears usually appear normal. It was the report of such cases by Treacher Collins[6] in 1900 that led Franceschetti to suggest that the entity be called "Treacher Collins syndrome." 3. Abortive. This shows only lid anomalies, as exemplified by the original cases of Berry in 1889.[7] 4. Unilateral. This rarer type shows hypoplasia on one side only. 5. Atypical. This form shows only some characteristics of the syndrome. Duke-Elder[8] believed that the linking together of these many apparently unrelated observations justified its designation as the Franceschetti syndrome, rather than the "Treacher-Collins syndrome."

This form of cranial dysostosis expresses a hereditary tendency, which is believed to follow an irregular pattern of dominant transmission.[9,10] Mann[11] attributed the malformation to a retardation in the differentiation of maxillary mesoderm in the embryo. This has recently been suggested to be secondary to the failure to form the stapedial artery during the sixth week of intrauterine life.[12]

Blodi,[13] in his recent review of the developmental anomalies of the skull affecting the eyes, stated that the Franceschetti syndrome is not as widely known as it should be; therefore, this complete case is reported.

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Report of a Case

An 8-year-old boy was brought to the outpatient clinic to the Massachusetts Eye and Ear Infirmary desiring glasses to protect his exposed globes (Fig. 1).

The patient had been troubled by exposure and epiphora as long as he remembered. Recently there was a question of loss of vision.

He was the third and youngest child in a family previously free from congenital anomalies. His prenatal course, birth history, excluding 36 hours of difficult labor, and neonatal period were uneventful.

Multiple congenital anomalies, involving the ears, eyelids, and palate, were present at birth. Surgical repair of the cleft palate was undertaken when he was 3 years old. He was provided with a hearing aid shortly thereafter.

Physical examination of this slender, healthy, alert, and cooperative boy revealed palpebral fissures which had an anti-Mongoloid slant (Fig. 3). Symmetrical colobomata of the lower lids were prominent at the junction of the inner three-quarters and the outer one-quarter, where there occurred angular deviation (bending up of the lower palpebrae), with resulting ectropion and epiphora. Eyelashes were found in the upper lid and the outer one-quarter of the lower, i. e., over the sensory distribution of the ophthalmic branch of the trigeminal

Figure 1

Figure 2

Figure 3

Fig. 1.—Front view. An 8-year-old boy with anti-Mongoloid slant of the palpebral fissures.

Fig. 2.—Lateral view. This profile depicts ear malformations, apparent prognathism due to a small mandible, and extension of hair down over the cheek.

Fig. 3.—Left eye. This enlarged view illustrates angular deviation of lower lid, lack of differentiation of inner three-quarters of lower lid, and a small dermolipoma near the nose.

nerve. In the area supplied by the maxillary branch there was an absence of the lacrimal papillae, a lack of Meibomian glands, and only a few sparse lashes. The vision in the right eye was counting fingers at 10 ft. and in the left, 20/60−.

His profile was characterized by a "parakeet" nose, fish-like facies, a receding chin, and a distinct tongue-like projection of hair down over the cheek in front of the ear (Fig. 2). A prominent dimple on the right and a smaller one on the left were present between the ears and the corners of the mouth.

The ears, set slightly low, were rudimentary pads which showed poor development of the pinnae and cartilages with crumpling forward of the helices. There were no external auditory meatuses; the loss of approximately 10 db. bilaterally throughout the speech range was attributed to their absence.

There was marked hypoplasia of the malar bones. Small dermolipomas were present on the nose. The bridge of the nose was wide, and there was a shift of the nasal septum to the left. His speech was indistinct, with a nasal tone. Micrognathia was present, as were macrostomia and a high-arched palate which showed the scar of surgical repair. The teeth were distributed irregularly.

The remainder of the physical examination was normal.

Summary

A review of the literature and a case of the complete form of the Franceschetti syndrome are presented.

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A Bibliography of the History of Ophthalmology

1955 and 1956

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In the March, 1956, issue of the A. M. A. Archives of Ophthalmology the first bibliography of this series appeared. Unlike the other ophthalmic subjects which are reviewed in this journal, the history of ophthalmology does not lend itself readily to the annual review type of article. The field, embracing as it does all the aspects of the specialty and its allied sciences, is too broad. For this reason, the form of a bibliography is used to bring to the attention of interested readers the large amount of work done in this field.

Over two hundred titles taken, for the most part, from readily available medical and scientific journals and books are listed under various subject headings. The titles are translated into English, with the original language indicated by a capital letter at the close of the reference. Standard abbreviations are used for the journal names. The period covered by the bibliography, 1955-1956, saw the re-publication of several classics of ophthalmology. These are listed under the appropriate subject and after the name of the editor who was responsible for their appearance and translation.

By using the form of a bibliography I deny myself the privilege of evaluating the material for the reader. In spite of this restriction, the following brief recommendations are made for certain papers which were outstanding works of scholarship and writing. For the complete titles the reader is referred to the appropriate section in the bibliography.

One of the most scholarly works to appear during the period was Edward Rosen's paper on the invention of eyeglasses. Only the introduction of new material can possibly shake his conclusions. Equally thorough was the work of Raiford on the development of the perimeter. For an amusing and informative tale the reader is urged to spend some time with Walls as he attempts to trace G. Palmer and his theory of color vision. In his chapter on keratoplasty Paton states that his work on the subject is selective; yet he provides enough material to be the basis for a future definitive work. The origin of the cataract operation was explored by Esser and Bidyadhar. These two scholars, on opposite sides of the world from each other, arrived, as might be expected, at somewhat different conclusions. All the classics of ophthalmology presented by Lebensohn should be read. In the field of biography recommendations are made for the study on Ibn-al-Haitham (Alhazen) by Sa'di, the life of Bartisch by Tower, the personal recollections of Verhoeff, and the papers on Jonas S. Friedenwald by Frankfurter, Wolman, and Woods.

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Librarian, Lucien Howe Library of Ophthalmology, Harvard Medical School, and Massachusetts Eye and Ear Infirmary.

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Case Reports

Melanosarcoma of the Choroid with a Long Period of Survival

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Melanotic sarcoma of the choroid is not rare or unusual and has been extensively reported in the literature. We believe the following case, in which the left eye was enucleated for this condition, is of interest because of the unusually long period of remission that followed before the patient succumbed to generalized metastases.

Report of Case

A white woman, aged 78 years, had had an enucleation of the left eye on July 28, 1929, when she was 52 years old, at Harper Hospital, performed by the late Dr. Walter Parker. She lived a useful life following this operation and succumbed to generalized metastases just 4 days less than 26 years later. Recurrence was first suspected in January, 1955, when she noted weakness, loss of appetite, and weight. She was hospitalized for evaluation of her condition and for care of diabetes that had developed in 1933. During this admission various studies, including gastrointestinal x-rays, were made, all of which were nonrevealing. She was readmitted March 21, 1955, with right upper abdominal quadrant colicky pains, anorexia, excessive gaseous eructations, and further weight loss. She was not jaundiced. The liver edge was palpable at the time of admission, and there was gradual increase in size, with extension to the umbilicus. The spleen and kidneys were never palpable, nor were there palpable nodes. It is significant that there was a positive test for melanin in the urine. Usually the liver is the first organ to be the site of metastasis, but terminally all organs of the body may be involved. In a patient who has had melanotic sarcoma of the choroid, examination of the liver and superficial nodes for enlargement should be made with regularity, since here may be found the first evidence of recurrence.

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Following is a summary of the gross and microscopic autopsy findings.

Aside from the general emaciation, there was a small nonpigmented skin papule on the right upper anterior chest which measured 0.75 cm. in diameter. Several irregularly outlined, slightly raised, partially pigmented papules were found on the skin of the left upper abdominal quadrant; the largest measured 1 cm. in diameter. The left eye was absent, and the orbit was clean.

The parietal and visceral pleural membranes were of normal thickness, smooth and glistening, but there were several subparietal blebs bilaterally, and these consisted of soft black tissue reminiscent of wet soot. The largest bleb measured 0.25 cm. in diameter. Bilateral hilar adenopathy was marked. The involved nodes were discrete and soft, and the usual architecture was replaced by a soft black tumor tissue in which there were minute irregular yellowish areas interspersed within the pigmented mass. The lymph nodes along and adjacent to the thoracic aorta were similarly involved. One tumor-involved lymph node was adherent to the anterior superior parietal pericardium but did not involve that membrane. The lungs were edematous, and the heart showed all signs of arteriosclerotic heart disease.

In the abdomen there were numerous

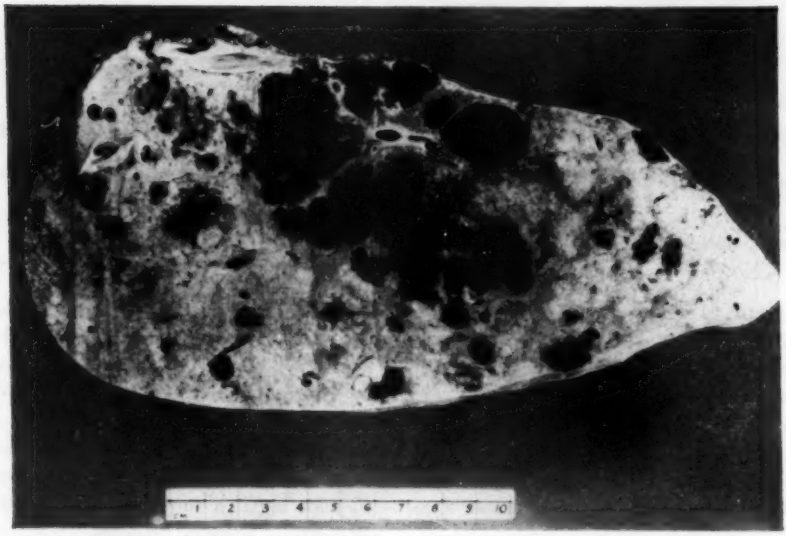

Fig. 1.—Pigmented melanoma metastatic in liver. (Reproduced from Mayer and Beitman,[8] *Harper Hospital Bulletin*, Detroit.)

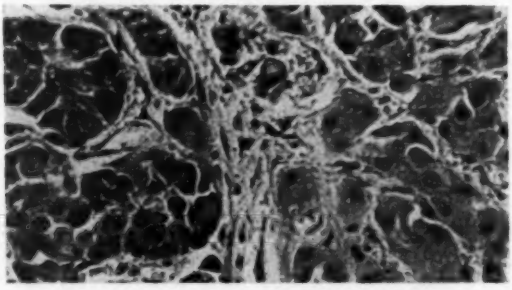

Fig. 2.—Alveolar arrangement of melanoma cells in liver. Note loss of cohesiveness; × 100. (Reproduced from Mayer and Beitman,[8] *Harper Hospital Bulletin*, Detroit.)

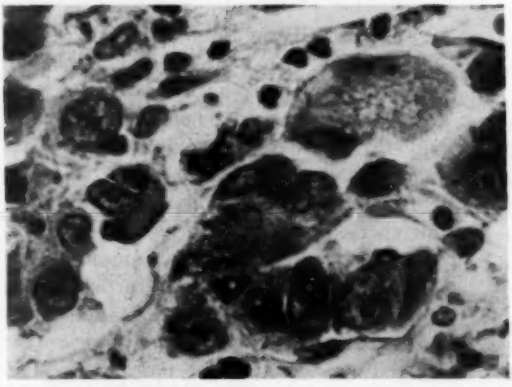

Fig. 3.—Large anaplastic melanoma cells showing multiple nuclei. Melanin may be seen in several cells; × 430. (Reproduced from Mayer and Beitman,[8] *Harper Hospital Bulletin*, Detroit.)

subperitoneal and mesenteric blebs of pigmented tumor tissue; the largest measured 0.15 cm. in diameter; these were most noticeable along the broad ligament and in the pouch of Douglas. The celiac nodes were grossly expanded by a similar tumor.

They were soft and discrete, and the largest measured 5 cm. in diameter. The para-aortic and iliac nodes were likewise involved.

The liver weighed 2200 gm. The capsule was raised by papule-like black tumor metastases. There were many large pigmented and a few relatively nonpigmented tumor deposits throughout the liver parenchyma (Fig. 1).

The spleen weighed 200 gm. There was a subcapsular pigmented tumor metastasis which measured 0.50×0.25×0.25 cm.

The adrenals weighed 10 gm. each. There were many flecks of black tissue within the medulla of each gland. Examination of the thoracic and lumbar vertebrae revealed similar minute pigmented tumor deposits.

All other structures, including those of the cranial cavity, were not grossly involved.

Histology.—Sections of all the abnormal tissues commented upon in the necropsy summary, with the exception of the skin papules, were composed of metastatic pigmented melanoma cells lying loosely within small aggregates (Fig. 2). The skin papules consisted of hyperkeratotic patches.

The metastases in all areas were similar, consisting generally of large pigmented cells which varied greatly in size and shape. The loss of cell cohesiveness was very apparent (Fig. 3).

The nuclei were large and varied greatly in size and shape. Multinucleated forms were common. Mitotic figures were uncommon (Fig. 3).

Large acidophilic nucleoli were a general and prominent finding.

A diagnosis of metastatic pigmented melanoma of epithelioid type was made.

Comment

In this case the microscopic report on the original tumor was melanotic sarcoma of the choroid, with no mention as to the type of sarcoma cells involved. Although the slides made at that time have been destroyed, we might speculate that the cells were of the spindle-shaped type in which the prognosis is the best. We mention this because at the time of enucleation, the pathologist, Dr. Plinn F. Morse, stated that the patient should have 20 years of life.

The classification of the cell types found in the melanotic sarcoma of the choroid is of interest because some prognosis can be made from the type of cells found in the original choroidal tumor. Wilder and Paul,[2] in a study of 2535 cases, mention the following cell types: spindle A, spindle B, fascicular, epithelioid, and a mixed type. Spindle A is least in malignancy; spindle B is somewhat greater; the fascicular is a degree higher, and the epithelioid is the most malignant. The fiber content of the tumor is also important, because if the tumor is slow-growing this may be an indication that the fiber production keeps pace with the tumor growth, forming a barrier about the tumor cells to prevent them from escaping into the blood vessels.

The degree of pigmentation is variable, but it is thought that with increased pigment content of the tumors there are more deaths.[1] Wilder and Paul[2] stated that approximately 80% of their series died within five years of enucleation. Three and one-half per cent lived 10 years or more. The longest case lived 21 years, while the average lived 44 months.

Berens[3,4] stated that the prognosis is better if the eye is removed early, before there is invasion of the ciliary vessels or extraocular extension. He states that a few patients have lived 17 years but that the majority live from 3 to 5 years. Those who have extraocular extension live six months to two years after enucleation. He also mentions that the prognosis is better in young adults under 30 years of age.

Lukens[5] reported a recurrence of a melanotic sarcoma of the choroid first seen in August, 1915, and operated on in 1918. Local recurrence in the orbit occurred, and the patient was reoperated on in 1931. No further mention is made as to duration of life after the second operation. In this case local recurrence occurred after 13 years. Newton[6] reported a man who had had an

enucleation of the right eye for melanotic sarcoma in 1923. In 1937 there was a local recurrence in the right socket. This patient survived for 14 years and possibly longer, as there was no evidence of general metastasis at the time of the local recurrence.

In our search of the literature we have been able to find but one case which survived longer than ours. Wilder,[7] in a discussion of melanotic sarcoma of the eye, at a meeting of the Chicago Ophthalmologic Society on Oct. 9, 1900, stated that some years previously he had seen in the laboratory of Professor Kundrath, of Vienna, a specimen of melanotic sarcoma of the liver in a subject who 32 years previously had had one eye removed for melanotic sarcoma of the choroid. Autopsy showed different organs were involved by the tumor. Dr. Wilder stated that he had never heard of survival for a longer period. In the literature this is mentioned as "Wilder's case." Actually, from Dr. Wilder's discussion, he had never had any contact with this particular patient.

The diagnosis in our case was made early in the disease, and operation was done promptly. At no time had the patient received x-ray or radium therapy.

Summary

A case of melanotic sarcoma of the choroid in which enucleation of the left eye was performed is reported because the patient survived for 4 days less than 26 years.

Dr. C. R. F. di Profio assisted in studying the pathological findings in this case.

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Serous Tenonitis

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This case is reported chiefly because of the rarity of the condition.

The patient, a 13-year-old school girl convalescing from a two-week period of an influenza-like disease, suddenly developed a swelling of the right upper eyelid, associated with ptosis and dark bluish-red discoloration in the pars palpebralis of the lid. In three days this lesion had largely subsided, but, in its place, the left upper lid appeared swollen and ptosed and the skin of its pars palpebralis was discolored a dark bluish-red. The left eyeball proptosed about 4 mm.; movement became limited and associated with deep orbital pain. In two weeks the proptosis on the left measured 7 mm. In three weeks the swelling and reaction in the left lid began to subside and, at the same time, a reaction again started in the right eye and continued to increase until the proptosis measured about 4 mm. Systemically, the patient complained of asthenia and indefinite aches and pains in the lumbar region, arms, legs, and occiput. The more-affected eye was painful at night and would keep the patient awake. There was no fever.

Antibiotic drugs administered systemically and locally appeared to do no good. At the third week of the disease, the patient was given 5 mg. of prednisolone twice a week and sulfisoxazole (Gantrisin), 1 gm., three times a day. A preparation of oxytetracycline and hydrocortisone (Terracortril Ophthalmic Suspension), 1 or 2 drops in each eye, four times a day, was also given. In 24 hours after this medication was started general symptoms were gone and the patient had a sense of well-being. In 48 hours the eye lesions showed definite improvement, and in eight days both eyes appeared normal.

Positive laboratory findings: Urinalysis twice showed traces of albumin. White cell count of the blood decreased from 22,000 to 8500; at first polymorphonuclear leukocytes predominated, but later mononuclear leukocytes predominated.

Electrocardiogram showed a sinus arrhythmia.

Significant negative laboratory findings: There was no eosinophilia, and no pathogenic parasites were found in the stool. Blood cultures taken for bacteria were negative. Blood smear showed no parasites. Radiograms of the nose were negative for pathology.

Differential diagnosis: 1. Our provisional diagnosis on the patient's first visit was angioneurotic edema. This, however, on the patient's second visit seemed very unlikely or secondary, because of the patient's general symptoms and the transfer of the swelling to the other eye.

2. A focus of infection in the nasal sinuses was then considered, but this theory had to be abandoned, as physical examination and radiograms of the nose were consistently negative.

3. Leukemia was considered but could not be confirmed by blood examinations.

4. Trypanosome disease was then considered but immediately dismissed, as the necessary vectors for this type of disease are not endemic in this country.

5. A metazoan infestation, particularly trichiniasis was considered but had to be given up. There were no petechial hemorrhages in the lesions or elsewhere. There

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† Dr. Pond died Dec. 24, 1957.

was no eosinophilia, and there was no fever. Stool examination for pathogenic parasites was negative.

6. Lastly, serous tenonitis was considered. This is an anatomical diagnosis, not an etiological one. According to Duke-Elders,[1] more than half of such cases are labeled as rheumatic. This appeared consistent with the rapid recovery of the patient when prednisolone, sulfisoxazole, and Terracortril Ophthalmic Suspension were given. The clinical development and the laboratory findings appeared consistent with the description of the disease.

Comment

The following clinical signs and symptoms were strongly suggestive of serous tenonitis: (1) sudden onset of eye lesions with subsidence alternating between the two eyes, (2) proptosis, (3) limited and painful eye movements, (4) serous lid swellings.

It would seem that the synovia in the orbits may be selectively affected in rheumatic conditions, just as they may be selectively affected in joints and tendons in such conditions. The reason for such localization cannot be given at present.

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Annual Reviews

Optics and Visual Physiology

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I. Some Books and Meetings

In last year's review on optics and visual physiology [300] I made short reference to the publication of Volume 3 of "Optique Physiologique," by Yves Le Grand. The present issue of it will properly start with a reference to the appearance of an English version of Volume 2 of this great opus.[1]

The year 1957 must be considered a happy one for optics and visual physiology for the appearance of still another book—a book such as seldom comes in a century—"The Vertebrate Visual System," by the late Stephen Polyak,[2] of the University of Chicago, including a study of "its origin, structure, and function and its manifestations in disease with an analysis of its role in the life of animals and in the origin of man, proceeded by a historical review of investigations of the eye." This is a great book and a grand book to read and cherish.

Another event that needs mentioning at the very beginning is the publication of "The Sheard Volume," a selection of writings of this distinguished author [3] on visual and ophthalmic optics, including some of his short papers, editorials in the now, alas, defunct *American Journal of Physiological Optics,* and his well-known monographs, "Dynamic Ocular Tests" and "Ophthalmic Optics." And a further important contribution to make the year a memorable one is Linschoten's [4] volume, "Structural Analysis of Binocular Depth Perception," a massive book with many interesting experiments offering a new theory, the "attraction theory," to replace the certainly outdated theory of E. Hering. While much of what the author offers as explanation of phenomena related to depth perception will not be acceptable to many, it can be hoped that the appearance of this volume may act as a stimulus for still further research.

A rather unusual textbook of optics by Ronchi,[5] originally published in Italian, in 1955, has been translated by Rosen and published in this country. The book might be a "revolutionary approach to the whole concept of optics," as the blurb assures us, "which redresses the balance of the science after centuries of its dehumanization by mathematics and physics"; as a text for ophthalmologists it is certainly of little use. (As often happens, a good review on a book gives more pleasure to the reader than the book on which it was written. This, I feel, is the case if one reads Fry's [6] excellent review of this book. Especially interesting is his discussion of the pitfalls in using the term "optics." The term has come to cover two quite distinct disciplines—the science of luminous radiation, or photics, and the science of vision, what Dr. Lancaster suggested should be called ommatology rather than physiologic optics, since "ophthalmology" is occupied by a profession and "optic" is essentially a term of anatomy. "Optics, the Science of Vision" seems to be a poor title for a book of questionable merit.)

Those interested in the history of ophthalmology will with pleasure read a supplement volume to *Ophthalmologica* [7] in honor of the 80th birthday of Prof. Arthur Brückner of Basel. The volume contains "Contributions to the History of Opthalmology" from the pen of distinguished

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From New York University Post-Graduate School of Medicine and the Manhattan Eye, Ear and Throat Hospital.

authors from many European countries. The student of optics and visual physiology will be proud once more to learn that among his "colleagues" he can count some of the most brilliant minds—names like Maurolico, Leonardo, Galilei, and Grimaldi, mentioned in Ovio's contribution on the history of ophthalmology in Italy; Roger Bacon, Peckham, Newton, and Young, in Duke-Elder's short contribution from Britain; Huygens, Donders, and Einthoven (of whom few know that he made important contributions to ocular and visual physiology), in the contribution of Zeeman from the Netherlands. Onfray's long contribution on the history of ophthalmology in France abounds with interesting bits of information on discoveries relating to our subject and with small but remarkably sharp pen-portraits, and the galaxy it presents of brilliant names, all well known, is almost dazzling. Arruga's contribution about the history of ophthalmology in Spain deals among others with some of the first books on our subject. One learns of a book, published as early as 1623, by Daza de Valdes, a notary of Seville, on "The Usage of Eyeglasses for All Kinds of Vistas," and for me it was especially interesting to learn that the first Spanish book on ophthalmology was a translation of the "Tractatus on the Diseases of the Eyes," by a Hungarian, J. J. Plenck, Professor of Surgery in Buda. The contribution of Rintelen, Brückner's successor, places the scientific work of his predecessor into the larger frame of German ophthalmology. Brückner is, as far as I know, the last living pupil of Ewald Hering. Fittingly, one finds ample material on the work of this great man and also his likeness printed.

The Annual Meeting of the Optical Society of America[8] (Columbus, Ohio, Oct. 17-19, 1957) cannot be left unmentioned in this review. Obviously, most of the material presented is beyond the scope of this review. There were, however, as always, several papers devoted to problems of visual physiology. G. A. Fry reported on the effect of red-adaptation on blue-green colors, confirming the well-known fact that exposing a blue-green stimulus to a red-adapted eye makes it appear supersaturated. Through the use of depurifying red and yellow stimuli it was possible, however, to locate this supersaturated color-mixture diagram. L. L. Sloan spoke about photopic receptors of the typical achromat. Her results suggest that both receptor mechanisms of the typical achromat have the spectral sensitivity of normal rods (not of high-threshold rods or of normal cones or even of "blue" cones). J. M. Enoch and G. A. Fry spoke about characteristics of a model retinal receptor studied at microwave frequencies. They determined the relative sensitivity and directional sensitivity of their model when irradiated (*a*) by a point source and (*b*) by a diffraction pattern. M. Alpern studied the variability of accommodation during steady fixation at various levels of illuminance. He found an almost fourfold increase of its variability when retinal illuminance was increased from 0.032 to 1000 trolands (in one-half log steps). G. Westheimer presented a theoretical treatment of retinal light distribution of circular apertures seen in Maxwellian view, especially studying the effect of the size of the pupil on intensity distribution in retinal images. L. A. Riggs reported about his well-known studies regarding visual effects of involuntary eye movements. As now known elimination of these movements causes vision gradually to fade away. "Involuntary saccadic movements play a major part in correcting the direction of fixation on a test object." H. R. Blackwell reported on general mathematical formulation regarding neural mechanisms involved in visual detection from experimental studies of target size and shape. S. Renshaw gave one of the dinner speeches on the subject "Visual Form Perception," which, if published, should be worth while reading. Of great general interest must have been the papers filling the greater part of one afternoon devoted to problems of optical detection of earth satel-

lites. (It seems that we were well prepared in at least one part of a greater project.)

A whole issue of the *Journal of the Optical Society of America* was devoted to work presented at the International Commission on Optics Symposium on Frontiers of Physical Optics, in Cambridge, Mass. Most of the papers read at this occasion are of no interest to ophthalmologists and are well beyond my grasp. But it is well to be reminded what a tremendous field "optics" has become. There were papers on the contribution of optical methods to nuclear physics, optical studies on thin films, studies on light-scattering in the atmosphere, on the polarization of sky light, on optical images, on microscopy, and others. Very exciting, however, for anyone interested in visual physiology must have been a paper by Barer[9] on refractometry of visual cells. Professor Wald has repeatedly described how modern anatomy will follow a path from the study of whole organ structures (the classic "anatomy") to the study of the anatomy of cells (the classic "histology"), finally to arrive at what is an "anatomy of molecules" within living cells. The amazing complexity of the rods and cones certainly can only make sense and become the basis for intelligent understanding of the visual process if "anatomic" studies are carried to this (one might call it) ultracellular level. One finds in this study, interestingly coming from the Department of Human Anatomy of Oxford University, that the outer segments, ellipsoids, myoids, polaroids of the rod and cone have different, measurable, and distinguishable refractive indices and that their difference from the refractive index of the intercellular substance into which they are submerged could account for the directed refraction and reflection of light within these cellular elements. While the author's conclusions based on these findings are all yet speculation, we will be enchanted by the vista offered by these speculations. One will learn that the author can, at last, offer a concept for our understanding of the Stiles-Crawford effect and, maybe, even of color vision. One has looked in vain, so far, for the three different pigments which our color experts would have been so eager to find in the cones, but possibly the differing refracting indices for different wavelengths are the long-sought answer! The wavelength-discrimination mechanism of the eye may work on this simple physical, rather than a complex chemical, principle.

Two other papers of the series should be at least mentioned; that of Sekera,[10] "Light Scattering in the Atmosphere and the Polarization of Sky Light" (a problem of interest to those interested in the spatial orientation of the bee), and another, "Transmission by Haze and Fog," by Arnolf, Bricard, Curé, and Véret,[11] French scientists working in institutions of optics, geophysics, and aeronautical research, obviously of interest to the flight surgeon and reconnaisance officer.

In another issue of the same journal one finds two interesting papers on a new branch of optics, called fiber optics. Studies conducted especially in Great Britain in previous years have shown that transparent fibers, assembled into bundles, are able to transmit a pattern of luminosities from one end to the other. In other words, if an image is formed upon one end of the bundle of glass fibers, a relayed image will be formed at the other end of the bundle. Fibers can be assembled in different patterns, e. g., into square arrays or more closely packed hexagonal arrays (cross sections of which strikingly resemble a pattern familiar to students of retinal physiology, the "mosaic" of visual cells in the retina). The student of retinal physiology cannot help thinking of an analogy with fibers in the optic nerve and radiation, which, after all, also relay the pattern of luminosities upon the visual cortex. To make the analogy even more stunning, it turns out from work by Kapany,[12,13] that the image relayed under static conditions is a poor one, as the ends of the component fibers

form an obtrusive pattern in the received image (reminding us of the fact that a "stationary" retinal image becomes obstructed). The resolving power of the fiber system becomes, as the author found, materially improved when the fiber bundle is used for "random dynamic sampling" of the optical image, just as the incessant movements of the eye contribute to its resolving power. "The individual end fibers are thus blurred out and the obtrusive pattern formed by them is destroyed." One cannot again help thinking of the beautiful experiments of Averill and Weymouth (1925), who found that the Vernier displacement is much better recognized in a moving pattern than in a stationary one.

The sixtieth gathering of the German Ophthalmological Society [14] (according to tradition, in Heidelberg) took place Sept. 3-6, 1956, but reports on it have not been available until the present year. The whole first day was devoted to physiologic optical and physical optical problems and questions relating to the treatment of strabismus. Count Arruga, of Barcelona, was the presiding officer. (Some of the papers are also mentioned in the appropriate sections of the present review; still, it seems worth while to keep this material together so that the reader may get a general impression of research work in visual physiology now going on in Germany.)

The first paper, by Monjé, dealt with the sensitivity of color-normal and color-abnormal eyes after preadaptation to colors, with use of red, green, yellow, and blue filters. None of these had, in normals, any influence upon color thresholds or absolute thresholds. Only in protanopics was there found a reduction of sensitivity of about 50%. But even in their case dark-adaptation was normal. Monjé's conclusion "that the sensation of white cannot be the resultant of the cooperation of different color-sensitive substances and that there exists a separate visual substance which is independent of color and not identical with visual purple" will interest all but diehard Helmholtzians. In protan-type color disturbances, this substance as well as some color processes must be affected.

Aulhorn and Harms discussed marginal contrast, stating that the sensitivity of the retina decreases on both sides of a contour. This decrease is the more marked (1) the greater the difference in luminance on the two sides of the contour, (2) the better the light adaptation, and (3) the farther in the retinal periphery contrast sensitivity is tested. Rosengren (in the discussion) thought that the decrease in contrast sensitivity is due to the irradiation of light within the eyeball and is related to glare.

Pabst and Echte reported on their studies of the time necessary for readaptation after "blinding" the eye with a standard amount of light during the course of dark-adaptation. The farther the latter has progressed, the greater is the time necessary for readaptation. The delay was especially marked in subjects older than 60 years.

Piper and Durchschlag studied the gradual emergence of different ocular performances in dark-adaptation with the adaptometer of Rieken and Meesmann. After 30 minutes in the dark, recognition of light and stripes, of a ring, of single small optotype, of several optotypes, and of graded reading test type was tested in this order, thus giving a profile of ocular function. In pathologic cases, some functions recover earlier than others. Relative central scotomas, amblyopias give characteristic profiles.

Cylinder retinoscopy gives false results in eyes with eccentric fixation, according to Rotter, since the examiner studies the light reflected from an extramacular area. He therefore produces a perimacular afterimage with the Cüppers euthyscope, thus forcing the subject to use central fixation during retinoscopy.

That a corrective glass has different effectivity when placed at different distances from the eye is well known. The usual conversion tables deal, however, only with the changing effectivity of distance corrections. Obviously, effectivity is also affected

when a near correction is placed differently. (My grandfather used to pull his reading glasses down his nose to see better.) Lindner, in his paper, and Graff, in his discussion of this paper, tried to fill in this gap in information.

Herzau reported on his experience of measuring aniseikonia. He found no greater size difference than 1% in emmetropia with normally functioning eyes. He also found that aniseikonia and anisometopia do not always show the expected relationship. He feels that the vision of young persons with aniseikonia should be fully corrected and at an early age, so as to prevent their getting conditioned to an anomalous sensory pattern. (It seems that Zeiss-Jena is now also ready to prepare corrective-size lenses, though at a seemingly prohibitive price.)

Of the next session, devoted to demonstrations, a few items will be of interest: Dannheim's elastic anterior chamber lens, which is only 5 mm. in diameter, has a weight of 8 to 9 mg. only, and is held in place by elastic slings of 0.1 mm. thickness, made of Supramid; a reconstruction of the Engelking-Hartung adaptometer by Engelking and Hartung, having several new features to improve its accuracy; another adaptometer by Schober; an anomaloscope with projection device for demonstration purposes by Schläfer and Jäger; a method to take colored stereoscopic photographs of the chamber angle with an electronic flash device, presented by Fischer and Van Beuningen; a very simple method for the measurement of depth in the structures of the front half of the eye, by Krannig; and, finally, studies on the visual field and the fusion ability after alcoholic intoxication, by Graff.

Among the papers read on the third day of the meeting is one by Schreck, who reported on 83 implantations of anterior chamber lenses into aphakic eyes (most of them had had monocular traumatic cataracts). The visual acuity (adequately followed in 71 cases) became better than after correction with conventional eyeglasses in 15 cases, was equal to this in 48 cases, and was worse in 8 (in these, owing to complications during the second operation). Stereoscopic vision was present in 43; binocular simultaneous vision, in 6, and fusion, in 15. Four lenses had to be removed; two were replaced by better ones. (One learns from the discussion that the authorities in Germany concede a loss of earning ability of 10% even after the successful restoration of binocular single vision and stereopsis with an anterior chamber lens.)

Barthelmess found that only in a small percentage of cases of monocular aphakia does binocular vision restore itself spontaneously. He recommends intensive orthoptic and pleoptic treatment before and after implantation and performs muscle operations if the divergence is greater than 5 degrees or if a vertical or rotary strabismus shows itself after implantation. He does not always choose the anterior chamber lens which gives best distance vision. He finds it more important that the usual activities be carried out without additional glass correction. The choice varies according to the patient's occupation. (Obviously the problem of the monocular aphakic worries German ophthalmologists as much as us, but they also have become more liberal in their indication for the removing of a cataract while there is still good vision in the other eye.)

Walser had good results with micro contact lenses and also with anterior chamber lenses. (He uses the Dannheim type mentioned above.)

Another paper read in the last session devoted to various clinical subjects merits to be mentioned as a kind of *curiosum:* Selle reported that hyperopes have small slit-shaped cerebral ventricles, difficult to fill during pneumoencephalography. Myopes have, he found, large ventricles which make this procedure easy; the drainage system of the cerebrospinal liquor is in their case well developed. ("How about

people with anisometropia?" asked the venerable Professor Lindner in the discussion. The essayist did not know the answer.)

Several papers of the meeting of the East-Central Section of the Association for Research in Ophthalmology[15] (Detroit, Jan. 7, 1957) dealt with problems that should be of interest. M. Alpern analyzed the question, "Does Relative Accommodation Exist?" and (much against what we would expect) found no record of movement of either eye when accommodation was induced by placement of minus lenses before the eyes. Thus, he feels that the commonly accepted explanations of Ames and Gliddon (that binocular single vision in this case is maintained with the help of fixation disparity) or of Fry and Morgan (that it is maintained by negative fusional vergence) are both not substantiated by the actual analysis of muscular potentials. G. A. Brecher, D. M. Winters, and C. A. Townsend used image alteration as a method for aniseikonia measurement and found that testing for aniseikonia is possible if the alteration is too slow for accomplishing binocular fusion but fast enough to permit subjective comparison of the size and shape of two images. J. H. Bruell reported on visual localization in hemianopics and normals and the concept of retinal local signs, referring to the famous studies of Poppelreuter, Best, and Fuchs on cases of brain injury after World War I. In an interesting experiment he found that the subjective straight-forward direction can be disassociated from the symmetrically converging foveas in normal subjects as well, if visual details are so arranged that only one occipital lobe receives stimulation. L. K. Guth reported about visual perception as influenced by age (measured by a sensitometric method of refraction which permits the determination of the lens power required to achieve maximum visibility with standardized viewing conditions). He found that the visibility decreases progressively beyond 45 years and that in order to achieve the same visibility result stronger illumination is required in the older age groups. Of great interest will be a report by J. H. Prince on experiments with a new method of assisting uncorrectible subnormal vision. He found that with a specific type face and scientifically controlled interletter spacing, improvement in legibility was possible, which enabled subjects with 20/60 vision to read print ordinarily requiring 20/20 vision at the same distance. A study by E. Schmerl on perception and transmission of primitive sensory stimuli suggests that light stimuli might also be accepted by the trigeminal nerve. In rabbits with excised occipital lobes he found no changes in perception. L. E. Lipetz found a dual response of the Limulus lateral eye to electric stimulation, an "early" response with shorter latency than a "late" response, the former having a higher rheobase and shorter chronaxie than the latter. The "late" response occurred only when the cornea was cathodal; the "early" response could be evoked by both polarities. Studies of photoreceptor structures were carried out by J. J. Wolken with the help of electron microscopy. He postulates a schematic structural model on the basis of fine structure, concentration of proteins and lipids, and number of pigment molecules in the isolated photoreceptor. Electroretinographic changes in experimental visual-cell pathology, produced in rabbits, convinced W. K. Noell that the average b-wave amplitude was misleading in indicating the severity of retinal pathology except when visual-cell degeneration was strictly localized. In cases where the degenerative process was diffuse and in which the electric potential originated from visual cells with damaged outer limbs, the b-waves were higher than would have been predicted from the histologic changes. He feels that changes in b-amplitudes should be evaluated at least in relation to the b/a ratio.

At the meeting of the Midwestern Section of the Association[16] (Iowa City, March 20-31, 1957) there were also several papers presented which should have refer-

ence to visual physiology. R. C. Drews gave an analysis of the illumination technique of Cibis. The zones of discontinuity of the lens are appreciated with this illumination because of minute granules scattering oblique light. The scattering locally obliterates the microscopic dark field. C. Keller and F. W. Newell presented their studies of the corneoretinal potential. They found that it is not a useful test of the health of the retina. A. H. Riesen and K. L. Chow tested form and brightness discriminations and their interocular transfer in relation to early visual experience. (The authors mean "ocular equivalence" when they say "interocular transfer," but I don't quite know why.) Their well-known experiments on primates and cats showed that discriminative abilities can be separately learned through one eye or the other. "If one or both eyes are exposed only to diffuse light from birth, the first form discrimination learned with either eye fails to appear when the second eye is exposed." B. R. Nebel reported about the phosphene of quick notion. Several papers referred to the problem of accommodation, in which scientific interest has been active lately. F. Armaly and H. M. Burian studied changes in the tonogram during accommodation and during relaxation and found the C value significantly larger during accommodation. (Whether this represents a real increase in facility or merely an apparent one due to increase in ocular rigidity, the authors were not yet able to tell.) F. C. Sabin and K. N. Ogle reported on experiments with phenylephrine (Neo-Synephrine), pilocarpine, and physostigmine regarding their influence on the AC/A ratio and found no significant effect. (This makes an interesting contrast to some of their previous findings with homatropine, the application of which markedly elevated this ratio.) K. N. Ogle and T. G. Martens reported some of their investigations on the accommodative and the proximal convergence. D. G. Fleming studied the role of the sympathetic in visual accommodation and found, in the rabbit, increased hyperopia after stimulation and increased myopia after extirpation of the superior cervical ganglion. "A strong time correlation between the increase in accommodation and the fall in intraocular pressure was noted."

II. "Retinology" *

The facts accumulated on visual pigments, on their physical and chemical properties, and on their structure (especially on the remarkable isomerism which so often is the key to their function) have become a sufficiently large body of knowledge to fill a book of moderate size (Dartnall [17]). It is easy reading even for those not specializing in biochemistry (which, alas, cannot be said about many papers nowadays filling our "clinical" journals).

One of the most amazing achievements of the last few years in the field of retinal physiology was the measurement of photochemical reactions in the living eye. Some of the light entering the eye is absorbed; some is reflected and emerges from the pupil. The ratio of the emerging to the entering light depends on many factors. In the dark-adapted eye a larger fraction is used up for bleaching the retinal pigment and a smaller fraction is reflected. After light-adaptation the latter fraction increases. The fraction also depends on the wavelength of light, as of some wavelengths more is absorbed and of others more is reflected. One of the principal workers in this special field, Weale,[18] developed entirely new machinery for the fast registration of the absorption and reflection fractions of the total spectrum. Among the many new details reported one will read with interest that some confirm the existence of the dominator mechanism postulated by Granit, while others confirm Wald's data regarding the existence of an intermediary product, *m*-rhodopsin, in the

* Chemical, physical, and psychophysiological data related to the influence of light on the organ of vision.

process of reduction of rhodopsin to its final components.

Peskin [19] estimated the density of visual purple in the distal segments of the retinal rods of Rana pipiens and found higher values than previously reported—0.642 at a depth equivalent to the axial length of the rod (estimated in the average to be 52.1μ). This means, according to the author's calculations, that about 75% of the light incident on the rod segment is absorbed if its path is parallel to the axis of the rod segment. Since, however, retinal rods do not occur in the optical axis of the eye but are distributed peripherally, a beam of light will fall on the rods obliquely; it will, moreover, pass several of them and at an angle of incidence of 45 degrees. By this, absorption will increase to 90%. Thus, peripheral vision not only has the advantage of higher absorption because of higher pigment concentration in the rods (which are missing in the fovea) but also has the greater probability of light-gathering, owing to the oblique incidence of the light.

A paper by Wald [20] deals with the metamorphosis in the visual system of the sea lamprey. This beastly little vertebrate, whose impact upon our Great Lakes fisheries has lately become a problem of some magnitude, changes its habitat twice during its lifetime, traveling from streams toward the ocean and then back to spawn and die. Its visual pigment changes, anticipating these migrations, and Wald found that it is based on rhodopsin and vitamin A_1 during downstream migration and on porphyropsin and vitamin A_2 in upstream migration. He believes that porphyropsin must have been the primitive vertebrate pigment, and this is consistent with the view that the vertebrate stock originated in fresh water.

The visual pigments in the rhabdomeres of the lobster and the visual system of the alligator were studied by Wald and associates.[21,22] The eyes of the former contain rhodopsin, with maximum absorption at 500 mμ. On irradiation, the extinction rises and becomes maximum at 490 mμ. The photoproduct finally goes over into a mixture of retinene$_1$ and opsin. The retina of the alligator was also found to contain rhodopsin. The main peculiarity of this rhodopsin was the quickness with which it was synthetized from neo-*b*-retinene and opsin. Rod-adaptation in the alligator, measured electrophysiologically, is as fast as cone-adaptation in frogs, in mammals, or in birds.

Two of Professor Wald's associates, Goldsmith and Philpott,[23] in a new magazine of which even the title is awe-inspiring (*The Journal of Biophysical and Biochemical Cytology*), have published a beautiful example of a new type research into intracellular microstructures, a description of the compound eyes of the flesh fly and the dragonfly, as seen through the electron microscope with magnifications up to × 32,000. There are seven rhabdomeres forming the rhabdom in the center of a single ommatidium of the compound eye, and these rhabdomeres have an amazingly complex structure which resembles that of the outer segments of vertebrate rod cells. This justifies the authors' suggestion that the rhabdom may be the site of photoreception as well as the organ for analyzing plane-polarized light—not the part which has been called "retinula."

The anatomy of the invertebrate eye was the subject of an interesting discussion by Lipetz [24] and Noell [25] after the presentation by the former of a beautiful study on the electric stimulation response of the lateral eye of the horseshoe crab, the favorite subject of experimentation of Professor Hartline and his school. Lipetz found two distinct response mechanisms—an "early" mechanism had the rheobase of 2.8 ma. and a chronaxie of 2.4 milliseconds; the respective values for the other, the "late," mechanism were 0.6 ma. and 300 milliseconds. When the cornea was cathodal, the electric current stimulated both mechanisms; when anodal, only the "early" response was apparent.

I am not sure of the existence of any evidence to substantiate the following piece of biologic speculation: Zagora[26] (in a paper discussing the biologic evolution of the organ of sight and of the oculomotor system along strictly Darwinian lines) states that: "Whenever a group of vertebrates swung from diurnality to nocturnality in order to escape diurnal predators ... there preceded a conversion or transmutation of most of the retinal cones into rods containing visual purple." We learn from the same paper that the four lateral eyes of the spider "serve for the estimation of distance and for near vision while the four main eyes serve for distance vision." Studies of 50 human embryos have convinced the author that "unconjugated eye movements probably appear already during the ontogenetic development." The evidence is meager, though the statement is most probably true. (One wishes that the amazing technique of Minkowski for study of the plantar reflex of fetuses would be applied to clarify the ontogenetic history of ocular rotation.)

Shikano[27] studied the validity of Ricco's law under photopic conditions and also for a red stimulus in scotopic vision. This law is generally attributed to spatial summation and is said to be due to the converging of rod impulses into a single optic nerve fiber. Since, however, Shikano found it valid under the just-mentioned conditions, he feels that simple spatial summation cannot account for it. (Shikano offers a new explanation in which the negative central scotoma in dark-adaptation plays some role, but this explanation is not quite clear to me.)

One of the classic problems of visual physiology is the relation between the minima of luminous energy, stimulus area, and stimulus duration which are able to produce threshold sensation. Nolan[28] replotted some of pertinent data of previous authors in terms of energy rather than luminance. He concludes from the curves obtained by this method that, within limits, absolute threshold depends on constant energy density at the retina and that in plotting the relation between energy and area it is the area as determined by aberrations which counts.

The measurements of McDougall (1904), Martius (1902), and Exner (1868) on "action time" (the least time during which a light of given intensity must act upon the retina in order to produce its full effect, i. e., to elicit a reaction of highest intensity) were recalculated by Allen[29] in terms of logarithms of intensity (I) and plotted against action time (A). He found that all curves satisfied an equation

$$A=k \log I+C$$

though the constants k and C were different for the different observers. This equation is just a special case of, and identical in form with, Fechner's logarithmic law of response and shows that action time decreases with increase of intensity within the limits of 0.2 to 0.03 second, the former value being the action time of minimum perceptible light. The classic measurements of Swan (1849) and Charpentier (1887), who found that action time was independent of intensity and had a constant value of $\frac{1}{8}$ to $\frac{1}{10}$ second, were obviously inaccurate.

Schubert[30] examined the influence of a large parafoveal surround (20 degrees in diameter) upon the light threshold of the fovea and concluded that the simultaneous contrast effect is a function mainly of the photopic system. He chose the increase of threshold in the fovea as a measure of the contrast effect and found that between this effect, K, and the brilliance of the surround, I, there was a relationship which, within an area of 6 log units, could be expressed by the following equation:

$$\log K=0.6 \log I+C$$

He thinks that the contrast effect finds its explanation in inhibitory processes in the synaptic layers of the retina.

Ronchi and di Francia,[31] of the Italian Instituto Nazionale di Ottica, studied the influence on vision of spatial and temporal gradients of luminance. They feel that the

so-called Mach bands (the peak and depression, respectively, in the subjective brightness on the two sides of a contour) are the expression of cone function. They are not perceived off the fovea or in blue illumination (which causes a different contrast phenomenon) and are readily appreciated in red illumination. They found in experiments in which the total energy of stimuli was kept constant and only their shapes were varied that the efficiency of a stimulus does not depend on its luminance level only but also on the spatial and temporal distribution. The main effect is caused by the temporal gradient, and both the voluntary and involuntary movements of the eyeball transform spatial gradients into temporal ones.

Hick (1950), measuring the differential threshold for velocity of a seen object, reported an approximate correspondence to Weber's law. Notterman and Page[32] repeated the experiment and found that, if at all, the law holds only for a very small range of the usable range. In fact, Weber's fraction passes through a minimum of about 0.11 in the 1 to 3 degree-per-second region of the range of initial velocities.

Pecking response experiments were used by Blough[33] in a very ingenious manner to determine the photopic and scotopic spectral sensitivity of the pigeon for 15 wavelengths from 380 to 700 mμ. Complete dark-adaptation curves were also obtained for each of the wavelengths. The scotopic maximum was found to be at 500 mμ; the photopic, at 560 to 580 mμ. The data correspond well with the results of electrophysiologic studies on the pigeon eye and also with the absorption spectra of chicken rhodopsin and iodopsin and the sensitivity of the aphakic human eye.

Pirenne, Marriott, and O'Doherty,[34] in a small monograph, published their experiments to determine (more accurately, to be able to predict) night vision efficiency at low levels of illumination (obviously a more and more critical requirement in proper placing of certain personnel). They found significant correlation between visual acuity and perceptual ability and the absolute light threshold. Different persons just need different amounts of light to carry out the same visual task, and everybody has his own subjective coefficient K by which required quantities of light need be factored for comparison purposes. (The uncertainty of seeing in low illumination is amazing.)

While, of late, several British authors (Lythgoe, 1940; Roaf, 1930-1933; Wilmer, 1943-1946) have come to the conclusion that the rods play some part in photopic vision, Yonemura and Nango[35] conclude from their experiments that rods are inactive in photopic vision. They studied the phosphene elicited by an electric current of about 25 milliseconds duration, which, they believed, causes excitation specifically of the rods. The spectral distribution of the responses determined in this manner agreed well with the well-known scotopic sensitivity curve; the magnitude of the responses first increased with increasing intensity of stimulus light but finally decreased at a certain intensity and above it.

A study by Brown, Kuhns, and Adler[36] suggests that the opposite might also be true, viz., that even if the eyes remain dark-adapted, cone function manifests itself whenever stimuli of appropriate intensity are available. These authors studied the luminance thresholds required for the resolution of parallel-line gratings with color filters and neutral filters. The required visual acuities varied between 0.042 and 0.625 in seven steps. When acuity requirements were low, the necessary luminance thresholds for blue were lower than those for red. But wherever the resolution required a higher order of visual acuity the minimum necessary luminances were nearly the same for all colors, indicating that "luminance thresholds, measured in the completely dark-adapted eye depend exclusively on cone function if the criterion of the threshold requires a sufficiently high order of visual acuity."

This study seems to be of importance for the situations in which a person, e. g., an airplane pilot flying at night, is adapted to a level of low luminance but must occasionally read visual displays at higher levels of illumination. Light of shorter wavelength might, according to these results, be preferable when the required visual acuity is not high and, thus, the necessary luminance is very low.

(To show that there is a transition from rod vision to cone vision as visual requirements and required luminances increase, the authors fitted double curves to their data. Their assumption is entirely reasonable. Still, an unsophisticated analyst cannot help but feel that to the scanty data—five or six to each curve—a simple curve could have been fitted in most cases just as well. Fitting of "expected" curves to insufficient data is becoming a dangerous scientific habit.)

Nebel [37] describes a probably common but so far only incompletely recorded entoptic phenomenon, the "phosphene of quick eye motion" or "flick phospene." He ascribes it to an instantaneous and transient deformation of the posterior surface of the vitreous due to inertial lag when the eye is suddenly "flicked." It occurs only in the dark-adapted and rested eye. The 7 subjects, out of 100 questioned, who were able to observe this phenomenon were all over 40 years of age; it is possibly a sign of the normal slight shrinkage of the vitreous and related possibly to Moore's "lightning streaks." (The author himself has small posterior vitreous detachment between the disc and macula in each eye.)

Haidinger's brushes are the subject of an extremely interesting study by Halldén.[38] One is not ordinarily aware of the complexities of the problem they offer, and most ophthalmologists are content to know that the phenomenon is connected with the ability of the foveal region of the eye to analyze the plane of vibration of polarized light. Different structures have been ascribed this analyzing faculty—Müller's fibers by Helmholtz, Henle's fibers by several other authors, and the retinal receptors by Gullstrand. The color of the brushes was assumed (by Helmholtz) to have something to do with the yellow pigment of the macula. Against this assumption many objections have been raised, and Halldén concludes that it cannot serve as an explanation. The dichroic character of the receptors to blue light or the dichroic character of the hypothetical blue receptors of the retina has been offered as another explanation for the contrasting yellow and blue colors of the brushes and their background. Halldén finds several valid objections against this explanation. Since blue and yellow, however, are complementary colors and the angle between the yellow sheaves and the blue hyperbolas is 90 degrees, Halldén concluded that the phenomenon might also be caused by interference. He constructed an ingenious model to show that when white light passes through a retarding plate and an analyzer the emergent light is colored. He showed, furthermore, that by inserting a retarding plate between a polarizer and the eye, the color of Haidinger's brushes can be changed. He thus feels rather confident that the coloring of Haidinger's brushes is an interference phenomenon. As to the analyzer in the retina, he feels that the retinal receptors themselves are its most likely site and that the retarding plate most probably consists of Henle's fibers.

Humphrey and Murgolo,[39,39a] using electrically generated phosphene responses, found that "increased intraocular pressure causes patients to report phosphenes having hues of longer wavelengths of the spectrum, while electrical stimulation of the optic nerve tracts or end organs of the normal eye results in reports of bluish white phosphenes." Twenty-two "visual cases" were tested; rather unsatisfactory case histories of three are published. In another paper this phosphene test for glaucoma was "extended to detect impairment of the retina or optic nerve by the simple procedure of

asking the patient to describe the form of the phosphene in addition to the color." In all cases showing macular loss a central dark irregular dark area in the phosphene was reported. The five skimpy case histories are unconvincing.

Urayama [40] found that the Maxwell spot, an entopic phenomenon usually thought to be caused by increased absorption of purplish light by the foveal pigment, disappears in the early stage of central chorioretinitis, returning soon in the course of convalescence. Its disappearance paralleled the decline of the red process in the fovea. On the basis of electrophysiologic findings, the author is rather inclined to accept the hypothesis of Walls and Mathews, that its origin is to be sought in the photoreceptors themselves. Testing squint cases with amblyopia, he found the spot to be shifted outward in exotropia, inward in esotropia, and up or down according to the vertical component of the strabismus. The shift measured from 20 minutes to 1 degree 40 minutes.

Many years ago (1940) Comberg suggested some simple means for the clinical study of one of the most important but neglected aspects of visual performance, namely, the light sense. In a new paper [41] on the subject several improvements of his technique are offered. (An electric ophthalmoscope, or the ophthalmoscope lamp, is all one needs as a measuring instrument. The improvements offered in the present paper are a ruler to measure distance and a plastic opaque contact lens to diffuse the light that falls upon the eye.)

"Modern Problems in Ophthalmology," a new Swiss publication, offers a good résumé of newer work on the light sense and on problems of dark-adaptation by Hamburger.[42] Interest in these subjects is not as lively as it was during the war. Still, many questions of great practical and clinical significance have been brought nearer solution. Of these, visual acuity and accommodation in dark adaptation, so-called night myopia, and the scotopic visual field are mainly discussed. Hamburger is an enthusiastic propagandist of the Goldmann-Weekers instrument, explains its many-sided usefulness but is not oblivious of some of its shortcomings, and gives good suggestions for further improvement. Of newer procedures for the study of the light sense he finds only Cibis' method of examining retinal local adaptation and Goldmann's sciascotometry worth mentioning. Interesting are his remarks on depth perception under scotopic conditions which seems to deteriorate beyond the measure of lowered visual acuity. Among the pathologic conditions which influence the light sense, Hamburger gives especial attention to the temporary blindness caused by pressure on the eyeball and anoxia. Both, he feels, affect the retinal neurons rather than the receptors and the retinal rather than the uveal circulation. In spastic conditions of the retinal vessels and retinal venous thrombosis, he finds tolazoline (Priscoline) injections of definite advantage. The improvement of visual acuity indicates that these pathologic processes disturb the retinal neural structures rather than the receptors. In "retinitis serosa externa," on the other hand, one finds disturbances of the light sense (sensitivity to glare and increased local adaptability). This one will rather attribute to lesions of the sensory epithelium via lesions of choriocapillary circula- which via choriocapillary circulation it, of course, also is dependent on blood circulation. Return of good visual function after retinal detachment indicates rather great independence from this factor. Diminished sensitivity to light, especially diminished contrast-sensitivity in cases of incipient cataract, are well influenced by doses of vitamin A with vitamin B_2, nicotinamide, and ascorbic acid. Commenting on the relationship of automobile accidents and disturbances of the light sense, Hamburger quotes the amazing report of Carrol (1953), who found that persons with congenital night blindness had little trouble or few accidents driving at night. Only profes-

sional drivers of large vehicles should be subjected to tests of the light sense. Glare will often cause accidents by veiling objects in the path of the driver, without any disturbance of the light sense. Light of longer wavelengths causes less glare, a fact which should be known by designers of cars. People with retinal disease suffer much from glare, local adaptation, and lowered contrast-sensitivity. They need colored lenses which eliminate ultrared radiation even under artificial illumination. "Uropalglasses," by Carl Zeiss, are the best available protection.

A chapter by Dubois-Poulsen and Magis [43] in the same publication deals with the laws of summation, especially those of spatial summation (which is the only type the authors find of oculistic interest). It is actually the capacity for spatial summation that is analyzed whenever in perimetry test objects of larger size are used. It does not operate in the fovea, where "each cone is limited to a ganglion cell." The analysis of its disturbances has become easy since the Goldmann adaptometer became available. (The study of this important survey of a timely topic—which cannot be reviewed here in any detail—is heartily recommended.)

Berens' [44] contribution to "Modern Problems of Ophthalmology" on the role of the retina in the speed of perception opens an eye upon menacing vistas. "Studies of the speed of vision in relation to light speed in flight suggest that at a speed of 1800 m. p. h., the time required for recognition of an object would be a contributing cause for collisions. In space flight, the situation is intensified by the time lag of controls. . . . Increasing and decreasing accelerations produce illusions of apparent motion which disconcert the individual. . . . The high speeds already attained have surpassed the speed of vision . . . ."

We know from publications of Wald that aphakic eyes become sensitive to long ultraviolet light to the degree of passable form vision when the rest of us see nothing. This turns out not to be an unqualified blessing. The retinas of such persons seem to become over-light-adapted by wavelengths which normally are absorbed by the lens, and, as Schenk and Pfeifer [45] found, their dark-adaptation curves become subnormal. Nor is this poor dark adaptation a symptom of age, as it could also be registered in a young aphakic person.

Erythema of the skin and epithelial lesions of the cornea are usually caused by ultraviolet C ($\lambda < 280$ mμ) and B ($\lambda = 280$ to 315 mμ), with maximum noxious effectivity in the region 230 to 260 and 300 mμ. Solar radiation is all but absorbed by the atmosphere below 290 mμ; only its shortest wavelengths cause conjunctivitides. The medicinal sunlamps radiate no ultraviolet C. The threshold for conjunctional irritation is three to four times higher than that of the dermal erythema. A photoallergic reaction to sensitizing drugs will sometimes cause ocular reactions to ultraviolet A ($\lambda = 315$ to 400 mμ) and even to visible light up to 500 mμ. Ullerich, Wulf, and Wiskemann [46] describe such a case, one in which chlorpromazine (Megaphen), a phenolthiazine derivative, was at fault. Their efforts to detect the noxious agent make a medical detective story, one worth reading.

Several teams of workers in Switzerland continue to determine standard curves for the adaptometer of Goldmann and Weekers. Fankhauser and Schmidt,[47] working in Goldmann's clinic, used a standardized course of preadaptation and used Landolt rings as test objects to determine (1) absolute threshold, (2) contrast-sensibility, and (3) visual acuity as dark adaptation went along. Standard curves for different age groups were set. Contrast was varied from 10% to 100%. The visual acuity determination followed a principle established by Novak, inasmuch as the time was marked when the position of the gap in a Landolt ring of size 5/200 was recognized.

Studies with Comberg's Nyctometer showed that older persons need a longer time in the change from light to dark to regain some set acuity of vision.

Similar standardization work was carried out by Böhringer,[49] while Dieterle, Gordon, and Abt[48] determined the standard curve and the 90% fiduciary limits of dark adaptation with the same instrument, using a new statistical approach.

(Though not at all belonging in this review, it should be mentioned that the possible untoward effects of chlorpromazine, nowadays one of the most generally used forms of medication, upon ocular functions have undergone careful scrutiny by Baumann.[50] The paper is worth reading. The patients were examined for dark adaptation and color vision; visual fields were determined, and the ocular fundi were studied. Baumann's results are encouragingly negative. The Goldmann perimeter and the Goldmann-Weekers adaptometer seem to be routine examining instruments in Switzerland.)

Gunkel and Bornschein[51] constructed an attachment to the Goldmann-Weekers adaptometer which makes automatic recordings possible. This additional feature provides for better standardization of the test. The curves are continuously recorded and with considerably more detail. Above all, the "break" in the dark-adaptation curve can be determined with greater accuracy. In extremely passive patients some difficulties may arise from this modification in technique and the conventional technique with the element of personal supervision by the examiner may give better results. Whenever this is the case, the automatic intensity control can be switched off, and the test can be conducted in the usual manner.

Mote and Forbes[52] measured the course of dark adaptation after preexposure to light. This has already been previously done. However, previous experimenters usually used constant intensities or intermittent light, while these authors used light which increased from zero to a maximum or decreased from maximum to zero in a continuous manner. They found higher initial threshold values when the preadaptation light increased in intensity. It also took longer in these cases to reach the final minimum threshold.

Smith and Dimmick[53] studied the influence of "light history" upon the course of dark adaptation. They found that light adaptation is not, as generally held, completed after a few minutes, since even after 15 minutes of light adaptation no stability of the scotopic mechanism was obtained. Considerable light adaptation time (up to 20 minutes) was required before the differential effects of the initial adaptation levels disappeared.

Fang, Hall, and Hwang[54] tested the dark adaptation of two subjects after preadaptation to 200 millilamberts for 15 minutes in a Nagel adaptometer with a test field of 3 degrees, 15 degrees above the fixation point, and found that intake of 0.6 to 10 mg. of carbachol (Carcholin) improved dark adaptability. In the toad, injection of 1.0 cc. of 0.001% of carbachol into the breast lymph accelerated regeneration of visual purple (as determined by both Garten's table and the extinction difference of retinal glycochole extracts measured at 500 mμ).

Helms, Krüger, and Strässner[55] found that light adaptation of one eye after dark adaptation of both increases the sensitivity of the second eye (which during the experiment is constantly kept dark-adapted). As the light-adapted eye readapts itself to dark again, the sensitivity of the other eye drops to its previous level. (Frequency of seeing was the criterion used to determine sensitivity. It was about 50% when both eyes were dark-adapted and increased to 70% in one eye when the other eye was exposed to artificial room illumination.)

Granger[56] obtained parafoveal dark-adaptation curves for a circular test field and a cross-shaped pattern, both of 3 degrees angular diameter and exposed for 0.2 second. The dark-adaptation curve for form perception (the recognition of the position of a

gap) had the same shape as the well known dark-adaptation curve for light detection, but it ran about 1 log unit higher than the latter. The fact is well known that "when the sensitivity of the eye has increased so that it can perceive light of a certain luminance it cannot discriminate form at that luminance." (The older literature differentiates a "light sense" from a "form sense" for this and similar reasons, but the logic of this differentiation is more than questionable.) As an explanation Granger refers to a theory of retinal organization by Pirenne and Denton (1952). According to this theory, a comparatively large number of independent retinal light detectors channel their excitement into a simple ganglionic transmitter of low transmittance threshold at low levels of retinal illumination. This accounts for the effect called spatial summation but offers only rudimentary form vision. At higher levels of illumination the same units will also fire ganglionic transmitters which are connected with only a smaller number of them but have higher transmittance threshold. These smaller units, offering a finer functional mosaic, are responsible for the better form vision.

An unusual study, by Seitz,[57] in connection with dark adaptation deals with the changes of the size of the pupil. He found that it reaches its maximum width after about two minutes. The size of the dilatation depends on age in the first place; the respective values in the first, fifth, and eighth decades of life are in the relationship 3:2:1. (A correction for pupillary size according to age in threshold measurements is obviously indicated.)

Marlow,[58] on the example of a patient followed for nearly seven years, shows that, in chronic simple glaucoma, the 1/1000/0.20 ft-c. field will notably contract, though the visual acuity and the 1/1000 full illumination field may remain practically unchanged. He finds visual field testing under reduced illumination in chronic simple glaucoma not only simple and practicable but more sensitive than normal perimetry.

An author whose findings have not always been corroborated by others, von Studnitz, recommended some years ago (1947) the use of an ester of dipalmitic acid (Helenien) to fasten and deepen dark adaptation. Many authors (among them some of international reputation) confirmed his findings. A new report by Pfeiffer[59] disclaims, however, all effectivity of this drug (*a*) in normals, to deepen their physiologic level of dark adaptation, and (*b*) in persons suffering from poor night vision, to improve on this defect. (The paper is also interesting from the methodologic point of view, as Pfeiffer did some of his work on the Engelking-Hartung instrument and another part on the Goldmann-Weekers adaptometer and is convinced of the superiority of the latter. A short but adequate description of the use of both instruments is also given.)

Studies of the electric activity of the retina have come into the foreground of ophthalmophysiologic research. This is evident not only from the great number of original contributions on many of its various aspects but also from the prominent place which "retinology" (the expression is to be found in Granit's address at the International Congress of Physiology in Brussels, 1956) has played in the gatherings of ophthalmologists and physiologists all over the world. In fact, an especial symposium on electroretinography[60] was held in Hamburg and its proceedings have been published as a supplement to *Ophthalmologica*, under the editorship of H. Sautter and W. Straub. Several of the contributions were also published in current magazines and are or have been mentioned in the present or last issue of this review. R. Granit, J. François, H. E. Henkes, and W. Straub spoke about more general topics; others spoke of special clinical or experimental problems or newer techniques.

A similar prominent place was given to problems of retinal electrophysiology in the already mentioned volume of "Modern Problems in Ophthalmology." A paper of outstanding clarity by Schubert[61] on the

electric activity of the retina is most heartily recommended to all needing an easily understandable and still accurate introduction to this more and more important aspect of clinical ophthalmology. He analyzes both the human ERG and the methods and results of microtechnique introduced by Hartline (1935) and Granit and Svaetichin (1939) and gives a short account of the amazing results of Ditchborn (1952) and Riggs (1953) with so-called stabilized images. He also gives an excellent account of the dominator-modulator theory of Granit. In a special section, the still-little-known studies on the electric activity of the iris and the ciliary muscle are also reviewed.

A paper by Henkes [62] on Electroretinography, read at the International Symposium on Physiology and Pathology of the Eye, in Iowa City, in September, 1954, has, with some delay, finally been published. It is still a rewarding introduction to this subject, though several newer ones have appeared since, as its main topic is the influence of retinal and general metabolic conditions on the electrical response of the retina. The author deals with the variations of the ERG due to variations of the direction, the intensity, and the wavelength of the stimulus and also with the influence of variable stimulus-frequency. He discusses the variations caused by changes in the state of adaptation of the retina and the variations caused by such experimental disturbances of retinal metabolism as occlusion of the carotids, decreasing the oxygen content of the inhaled air, and artificial changes of intraocular pressure (in the cat). Among the clinical conditions studied for changes in the ERG were diabetic retinopathy, perivasculitis retinae, commotio retinae, glaucoma, papilledema, optic neuritis, and disturbances of the general circulation. Interesting contributions were added in form of discussions by Burian, Schubert (Vienna), François (Ghent), and Best (Bonn).

As to the site of origin of the ERG, Svaetichin [63] believes it to be in the photoreceptors. The bipolar cells or the optic nerve have an electric activity of their own with a much slower rhythm which, besides, is more vulnerable. The rectangular pulse-like action of the L (or dominator)-type cones agrees with what is called the PIII component of the ERG. The "on-off" response of the chromoreceptors (or modulators) corresponds with the a-wave and the "off" effect, respectively, of the ERG. The c-wave might be produced by the pigment epithelium. In the well dark adapted retina only a b-wave and an "off" effect were recorded (at least in the fish), while the pure cone effect simulated the PIII component. The latency of the a-wave was 15 milliseconds and was independent of stimulus intensity, paralleling action potentials of simple cones; the latency of the b-wave was much longer, 45 to 75 milliseconds, varying with intensity, indicating that it is a rod response. Recording the b-wave of retinas subjected to gradually increasing adaptations to light, the author found a shift of maximum intensity toward longer wavelengths (Purkinje shift). According to the prevailing opinion, this change indicates gradual shift from rod to cone vision. In his opinion, the rods continue to act parallel with the cones even under strictly photopic conditions.

Readers not especially interested in ocular electrophysiology will be annoyed by the steadily increasing space occupied in ophthalmologic journals by papers on the esoteric subject of electroretinography. To them the study of details of a graph traced under an endless variation of conditions will seem rather pointless. Here then, is a fine paper by Goodman and Bornschein,[64] sparing in elaboration and exemplary in display, from which even the uniniated will easily learn what electroretinography can be used for. Excellent illustrations show the curves of dark adaptation and the ERG's of a totally color-blind and a congenitally night-blind subject (both women) contrasted with those of normal subjects under similarly varied conditions of adaptation and stimulus color and intensity. They found

that both the negative a-wave and the positive b-wave of the totally color-blind subject reflected exclusively scotopic activity. One will thus continue to feel justified to call such a subject a "rod monochromate." The positive x-wave of the night-blind subject reflected the expected photopic activity. However, the negative a-wave of this subject demonstrated both photopic and scotopic activity. The latter finding was somewhat unexpected, raising new questions which the authors have ably discussed.

Another paper by Bornschein and Goodman [65] deals with the negative a-wave. High-intensity stimuli of 6,000,000 millilamberts of about 10 microseconds duration show clearly that it has two components in the normal person (a_1 and a_2). The hump separating them was less pronounced in a totally color-blind subject and totally lacking in a night-blind one. The implicit time shortens with increasing stimulus intensity. The latency with highest stimulus intensities is as short as 2.6 to 3.0 milliseconds, and it was of the same order in the normals as in the two pathologic cases. The authors lean toward the explanation that the "break" splitting the a-wave into two portions is most likely due to an interrupting positive potential and does not indicate two separate (photopic and scotopic) negative potentials of different latency. The interrupting positive potential might be one of the several positive "small waves" which have been found to be superimposed upon the larger and so-far better-analyzed potentials.

Bornschein, Goodman, and Gunkel [66] varied the wavelength and the intensity of the light stimulus to study the relationship between the amplitude and the so-called implicit time (the interval between onset of light stimulus and peak of wave) of the scotopic b-wave. The amplitude increased with intensity up to a maximum of about 0.6 mv.; the implicit time varied between 60 and 140 milliseconds, in an inverted exponential relationship with the amplitude of the wave. (Implicit time was, e. g., between 120 to 140 milliseconds when the amplitude of the b-wave was 0.1 mv. and decreased to 60 to 70 milliseconds when the amplitude increased to 0.5 to 0.6 mv. It showed both a minimum and a maximum value.) Colored light stimuli had no specific influence on implicit time; it was influenced only by the luminous intensity of the stimuli.

Horsten and Winkelman [67] studied the effect of temporary occlusion of the aorta on the disappearance and reappearance of the ERG. The (positive) a-wave and the (negative) b-wave behaved differently, and the reactions were different a strong or a weak stimulus. With a (strong) stimulus of 50 lux the b-wave disappeared after 38 to 61 seconds, while with a (weak) stimulus of 1½ lux it was demonstrable as long as 3 minutes. The negative potential appeared only with the strong stimulus, and it disappeared only after three to seven minutes. After removal of the clamp it was this component which returned more quickly (after as short a time as 3 to 11 seconds). The b-potential returned much later and appeared stronger in the eye that received the weaker stimulus. In cases in which the occlusion lasted longer (up to 13½ minutes) restoration of the b-wave was imperfect. In eyes receiving the stronger stimulation an exaggerated c-wave became observable. Another fact that showed that the retina had suffered damage was the appearance of the so-called exhaustion phenomenon, the rapid decrease of the b-potential after intermittent illumination with a strong light.

Biersdorf and Armington [68] studied the ERG of the human eye as elicited by the abrupt replacement of a chromatic adaptation stimulus of five minutes with a test stimulus of about one second's duration. The adaptations were to red, yellow, green, blue, or "black" in a scotopic series and the same wavelengths with white added in a photopic series. The test stimuli were varied in steps of 0.5 log units down to the point of equality with the adaptation luminance. They found that relative spectral receptivity (measured by response amplitude from the

lowest point of the a-wave to the positive peak of the response) was strongly dependent upon the color and luminance of the adaptation stimulus, with adaptation to a particular color lowering sensitivity to the same part of the spectrum. They found evidence of at least two "spectral processes" with maxima near 620 and 500 mμ and found that the latter, a rod process, is capable of performing even in the light-adapted eye. The fact that the maximum of this process is comparable to that of visual purple "shows that the rod mechanism still functions under photopic conditions." The other process "has a peak consistent with the maximum of the cone photopigment but it drops off more sharply on either side of the maximum."

Mahneke [69] recorded the human ERG under still another variation of conditions, using as stimulus two successive flashes of equal duration but with varying dark interval between the two. He found that in the tracings from the light-adapted eye responses can be clearly distinguished if the dark interval is greater than 25 milliseconds. In the dark-adapted eye the necessary interval was 50 milliseconds. There were certain changes in the configuration of the second flash if the dark interval was between 100 and 850 milliseconds involving the a- and b-wave. However, the significance of this is still not clear, to justify more detailed reporting.

Brown, Hill, and Burke [70] studied the influence of hypoxia on the ERG, finding that the response to red light (the x-wave) was reduced more than 50% while their subjects breathed a nitrogen-oxygen mixture containing 9% of oxygen (equivalent to an altitude of 20,000 ft.). Recovery of this component of the ERG was not complete even after 10 minutes spent in normal air. This result contradicts, to some extent, the well-known findings of Schubert and Bornschein (1952), who reported no reduction of the x-wave in a hemeralopic subject. As mentioned earlier, another finding of these authors has lately also not been confirmed. It thus seems that there are still some contradictions in reports of reliable observers. Obviously, either the techniques of recording the ERG are not yet sufficiently standardized or different authors refer to different processes while using the same term.

Best and Bohnen [71] found that the so-called off-effect in the human ERG is only seen in light adaptation. With short stimulus durations and low intensities it becomes confluent with the on-effect and it becomes the dominant effect with very short stimuli. When stimuli have relatively long duration and high intensity, the off-effect is minimal. It becomes more prominent as their intensity decreases. Obviously, long or intense stimuli have an inhibitory influence already proved by Granit) upon this particular effect. The intensification of stimulation also increases the latency period of the effect; thus, even with short stimulus duration on- and off-effect become separated if intensity is increased. There is an inverse relationship between intensity and duration of stimuli to elicit a maximum off-effect. The authors feel that the off-effect, being related to the inhibitory effects of retinal illumination, is also related to contrast and afterimage phenomena in the psychophysiologic sphere. Moreover, this view also fits into broader and newer aspects of retinal physiology, since the inhibition of neuronal pathways and the shunt from one set of neuron chains to another set has lately become regarded as the essential feature in the transition from retinal dark to light adaptation.

Another paper by Best and Bohnen [72] deals with an alternating potential presenting itself in electric retinal tracings when intermittent light stimulation of high frequency (40 to 60 cps) is applied. Every second stimulus has a smaller effect. The authors explain this with a delay in the off-effect of every second stimulus, which finds itself partially neutralized by the following a-wave. The delay of the off-effect, in its turn, is caused by the lessened sensitivity

in the wake of the first stimulus. Since the second stimulus was not fully effective, the third stimulus, like the first one, finds a substratum of full sensitivity—thus the alternation.

Rendahl [73] made a study of the so-called x-wave, the positive potential in the photopic ERG, using a red stimulus. In dark adaptation the x-wave showed up as a small elevation preceding the b-wave. In moderate light adaptation the latter was suppressed and the x-wave appeared in its isolated form. The peak of it appeared at about 40 milliseconds independently of stimulus intensity. Very intense stimulation with electronic flash in the dark-adapted eye produced an ERG dominated by a large a-wave followed by a b-wave; at one-quarter of this intensity the positive wave split into an x- and a b-component. Successive further decreases in stimulus intensity led to disappearance of a- and x-wave, leaving the typical scotopic ERG. Normal x-waves could be obtained in the tracings from protonopes by use of a red stimulus of larger wavelengths than 625 mμ.

Rendahl [74] studied the ERG in 277 eyes of 250 patients with detachment of the retina. He found that the size of the b-potential decreases in relation to the area of detachment and that the mean b-potential before operation was higher in eyes in which operation later turned out to be successful. He also found that the b-potential of the other, "healthy," eye of his patients was, on the average, lower than that in normal persons. This difference was also present in eyes that were not myopic. His results thus seem to confirm the existence of a predisposition to retinal detachment. (Strangely enough, his observations were the same in cases of so-called idiopathic and of traumatic retinal detachment.) Interestingly, Schmoger, who studied the same question, found no definite correlation between poor prognosis and low preoperative b-wave.

Skeehan, Passmore, and Armington [75] described a case of retinitis pigmentosa, well-documented with visual fields and fundus photographs, and difficulty with night vision in which the ERG was normal or nearly so. "The ERG, then, cannot be relied upon to verify unerringly the diagnosis of retinitis pigmentosa."

In a group of cases of congenital glaucoma François and his group [76] found subnormal, absent, or electronegative ERG's. (They also found both segments of the dark-adaptation curve pathologically displaced.)

The ten Doesschates [77] (father and son) reported on the resting potential of the human eye in light and dark adaptation in a previous communication (1956). Now they have added some further data on the same subject. They found that the potential minimum (which always manifests itself in the course of dark adaptation after preadaptation to light) occurs after a longer interval if the intensity of the preadaptation light is increased. The wavelength of the preadapting light (red and blue filters were used) has no influence on the manifestation time of this minimum. In a case of congenital hemeralopia the resting potential remained the same for 30 minutes' dark adaptation in spite of preadaptation to 75 lux. (The latter observation differs from the one published by François, Verriest, and de Rouck [1956] in whose case of congenital hemeralopia both the absolute value and the drop of the resting potential during dark adaptation were found to be normal. Obviously, the two cases of hemeralopia belong to different types.)

Mahneke [78] continued his valuable studies to determine the c r i t i c a l frequency of flicker fusion (CFF) with varying experimental techniques. After he found out [300] that under conditions of continuous stimulation the flicker-to-fusion and the fusion-to-flicker thresholds are affected in different manners, he turned to a study of the variations of these thresholds under discontinuous stimulation. He now believes that discontinuous threshold determinations with a reasonably long exposure period (five to

six seconds) are the method of choice for clinical purposes. Determinations of continuous fusion-to-flicker thresholds can be equally reliable, but the proper rate here of accelerations becomes an added factor of concern. Continuous flicker-to-fusion threshold determinations give lower frequencies, and the values depend too much on the rate of acceleration.

Many authors believe that the mechanisms which determine the phenomena of flicker and fusion are chiefly situated in the brain. Recent studies concerning some peculiarities of the human ERG produced by intermittent stimuli lead to the conclusion that the limiting mechanisms which cause flicker and fusion must be in the retina itself. Experiments by Svaetichin [79] in which the frequency of the intermittent stimulus of constant intensity was doubled (e. g., to 20 from 10 Hertz) showed that under these conditions the amplitude of the individual cone responses became halved. An increase of stimulus intensity by 1 whole log unit was necessary in order to recover the original amplitude of the response. The author assumes that there exists a critical smallest amplitude of cone potentials which is necessary to evoke neuronal spikes. If the amplitude is greater than the critical value, the rhythm of the spikes is in accord with the rhythm of the receptor responses; if it is smaller, fusion occurs. Since with increasing stimulus frequency amplitudes have been shown to decrease in linear fashion, it becomes understandable why increase of stimulus intensity in logarithmic manner is necessary to increase them above their critical magnitude, thus preventing the fusion of the rhythmic responses. This brilliant hypothesis (which explains the well-known relationship between CFF and log stimulus intensity) does not, of course, exclude the possibility that in the perception of flicker and fusion other neuronal activity, at different levels of the visual pathways, above the level of the retina, also plays a role.

Kožoušek [80] made extensive perimetric flicker studies with an adaptation of the Maggiore perimeter. From his very complex, poorly presented, but otherwise excellent data one learns that the CFF increases to double when the illuminated surface increases by 180 and that it increases about 50% when a white instead of the gray perimeter is used. The CFF is highest some 25 degrees from the macula with stimuli of low intensity and some 20 degrees from the macula with stimuli of high intensity. In the macula itself it is higher with strong stimuli. In dark adaptation he found diminished CFF; this he explains, in a very convincing manner, by the decrease of threshold, which, in its turn, permits longer effective supraliminal stimulation by each and every flash. In amblyopia CFF was within normal limits both in the macula and the periphery. Comparing, however, the maculas of the normal and the amblyopic eye in the same person, he found the CFF in the macula of the amblyopic eye to be higher when illumination was low—as high as in the periphery of the normal eye. Thus, the amblyopic macula carries, so to speak, characteristics of the retinal periphery. When stimulus intensity was high and thus the normal foveal CFF was also high, amblyopic eyes presented the smaller values.

While experimenters interested in persistence of vision usually deal with the so-called critical frequency of flicker (CFF), the frequency at which fusion of alternated fields of differing luminances is experienced, Truss [81] investigated a less commonly studied phenomenon, the critical frequency of color fusion (CCFF), in other words, the frequency at which alternated fields of equal luminance but differing chromaticity are subjectively fused. The author contends that the reciprocal of these values (1/CFF and 1/CCFF, respectively) have greater biologic significance, as they are the actual measures of the persistence of vision. As CFF had been, CCFF was also found to be a function of luminance and the relation of log CCFF to log luminance indicates a linear function.

III. Color Vision

Professor François is one of the most amazingly fertile writers among prominent present-day ophthalmologists, one who publishes almost as many papers a year as many of us read, all of them well organized and (what is not always the case in French publications) appendaged by complete and reliable bibliographies. Several of the papers by him and his collaborators are reviewed in other sections of this paper. Here I want to report about a series of papers on color vision. The first [82] deals with a statistical study of 1243 boys of the region of Ghent (Belgium), among whom 8.61% were found congenitally color-deficient. Of these, 57% were deuteranomalous; 11.8%, protanomalous; 17.1%, deuteranope, and 11%, protanope. They also found general color weakness in 2.3%, and 0.8% had a tritanomaly. A number of interesting tables give comparisons with the data of other authors, separating Europeans and non-European races (in whom the percentage of color deficiency usually was found to be smaller). The 10th edition of the Ishihara charts served as the basis of classification. The Polack atlas and the Farnsworth polychromatic plate and dichotomous test were also used; the last word was that of the anomaloscope.

A paper of monograph size [83] deals with the acquired disturbances of color vision. Here again the scope is wide. The techniques of examination of color-normal and color-defective vision are so exhaustively treated that anyone needing an introduction into the subject will find this monograph a welcome source. One is pleased to see that the methods of testing introduced by Farnsworth are given their due place in the ophthalmodiagnostic armamentarium. Good clinicians as our authors are, they note that the acquired color deficiencies distribute themselves around a red-green or a blue-yellow axis—all efforts notwithstanding to force color vision into a trichromatic scheme.

Analysis of the color vision in a group of cases of congenital glaucoma by François and his group [76] revealed a tritan type of defect when examination was done with the Farnsworth dichotomous test in a number of the cases.

Another long paper by these authors [84] is a review of our present-day knowledge of the color vision of animals. There is a short introductory chapter on human color vision and a longer chapter on the different methods used to detect color vision in animals, while the bulk of the paper contains a compilation of data with critical remarks. This is followed by a chapter of theories on the phylogenetic development of color discrimination. Much of this is speculation by the very nature of things—but interesting speculation. The authors think that as some species were forced from daylight into nocturnal existence, cones might have acquired characteristics of rods. The opposite change might also happen. They do not believe that human color defects are an "atavism"; they believe them to be the outcome of chance mutation.

Polack,[85] the author of a French atlas for detection of color anomalies, tried, in a posthumously published paper, to rectify some inaccuracies in the construction of Maxwell's color triangle. This rectification is as belated as it is unnecessary. The work of the great Maxwell, about 100 years old, signifies the greatest step toward colorimetry as a science since Newton and has to be seen in its historic context. Modern colorimetric studies, incorporated into the well-known CIE diagrams, have long ago corrected the Maxwell color equations, remeasured the desaturations of mixtures and determined the correct locus of white in the color diagram. All this does not detract from the greatness of Maxwell's work, and we should not "rectify" a classic.

Birren,[86] one of our best known color scientists, published a paper on the role of vision, visibility, and color in highway safety which is certainly worthy of being read. That "it is one thing to be able to see and

another thing to be affected . . . by what is seen" is a good point to remember.

Simple experiments with highway signals showed convincingly that their legibility is only one of the many factors that will make a signal useful. "Color vision adds a necessary force of compulsion to the visual process." "The right colors will mark danger spots far more effectively than will signs containing words or legends." As a matter of fact, in experiments under usual driving conditions, Birren found that 86% of drivers did not recognize, e. g., that TOPS was substituted for STOP. Their primary reaction was to color and shape. A uniform color code (red for danger, yellow for caution, and white letters on green background for directional signs) should be generally accepted. A Government "Manual on Uniform Traffic Control Devices" has come up with the idea of using white lettering on black background for its "better legibility." Birren finds that this choice is the poorest possible. "Like space itself, black is hard to localize. . . . Being 'emptiness' or 'nothingness', it is most difficult to focus," while "color speaks all tongues."

Recognition of the color of monochromatic lights might become quite a problem when reading of safety signals of extremely low intensity depends on the color perception of a human operator. True, in good dark adaptation a few quanta of light are sufficient to cause perception. There is, however, a certain instability of response near threshold, depending on random fluctuations in the number and distribution of the stimulating quanta over the retinal receptors. Color recognition also depends on such fluctuations. The chance of observing something (a "light") is always larger than the chance of recognizing a certain color. That recognition of color must be extremely poor near threshold is apparent from studying the curves in an interesting paper by Bouman and Walraven.[87] One finds in this paper that at stimulation with light of, say, 580 mμ the subjects reported "white" (oftenest) but also "yellow," "green," or "red." Even at 640 to 660 mμ there were some "white" and "green" responses besides "red." Interestingly, the "green" response was always found more unstable than "red." The latter reaches nearly 80% probability when the stimulating light has a wavelength over 680 mμ, while the former never reaches even 60% with any wavelength and with any level of stimulus intensity. The authors conclude that an elementary sensation of "green" requires at least 3 quanta, while 2 are sufficient for "red." (It seems that choosing "red" as the danger signal was a good choice, after all.)

W. R. J. Brown[88] presented the results of another of his projects of almost gigantic proportions. Twelve observers were used, and their color-discrimination ability (sensitivity to small color differences) was studied around 22 loci of the chromaticity diagram. Whether the finding of somewhat smaller diameters of "error-ellipsoids" was worth the effort, I cannot tell.

A beautiful paper by Roelofs and Zeeman[89] deals with the importance of contours for the perception of brightness and color. Most of the experiments were carried out with rotating discs of various and clever design or in the haploscope and show that contours greatly increase the perceptibility of colors. Contours carry their surround with them. Their effectiveness is, in the authors' view, due to their optomotor effectivity. If this effect is prevented (as in the experiments with so-called stabilized images reported previously) optic localization becomes vague, and if it is not present, owing to lack of contours, optic localization becomes indefinite. (This type of experiment should be introduced into every basic course of visual physiology. It is simple; the material used is inexpensive and the young student will derive the greatest possible pleasure and benefit from having once experienced these fascinating phenomena.)

Some questions raised in this paper were further analyzed in a subsequent study. The authors[90] conclude that there are "three factors essential to the development of

colors, viz., physical light quanta, photosensitivity and time." They make the assumption that any color sensation is based on a physiologic rhythmic process, a theory as reminiscent of Troland's modulation theory as their results are of Fry's (1933, 1935) beautiful experiments on subjective colors. "The three-receptor theory of Young and von Helmholtz is rejected as improbable . . . in the basis of the phenomena observed."

Burnham, Evans, and Newhall[91] determined "the colorimetric specifications of colors having the same appearance" (made, in other words, color-matching experiments) after the observer was adapted to three different illuminants with one eye and to a standard illuminant with the other eye. From the data it is possible not only to measure the effect of adaptation but also to predict color appearance very accurately, at least under the studied different conditions of adaptation. "Theoretically there would be an advantage in being able to predict from the color appearance of a given object under a given illuminant its appearance under any illuminant." The authors' efforts to find "a satisfactory matrix" (or "fundamental" response functions, as the colorimetrists usually refer to them) failed, however, and they, correctly, suggest that either "the data may be inadequate or the hypothesis incorrect." They find that their data *were* "quite adequate from the standpoint of internal consistency. . . . As regards to general theory, however, evidence has been accumulating for a long time to show that the tricomponents (=Young-Helmholtz) concept cannot suffice by itself to explain all observations fully." Of course, "regardless of theoretical difficulties in applying a three component conception to the general prediction of color appearance, it works well for more specific predictions." (In fact, the usefulness of the Young-Helmholtz concept as a practical tool has never been questioned, even by those who do not happen to believe that it is correct.)

A team of scientists, including two of the just-mentioned authors, Newhall, Burnham, and Clark,[92] made further studies on color matching by comparing simultaneous and successive matches. This is a complex problem, and the literature on it (in which adherents of the Gestalt school were very active) is well covered. Successive matches in the authors' experiments essentially yielded higher purities and somewhat higher luminances. This was to be expected and is a direct consequence of the "selectivity of memory."

Sanders and Wyszecki,[93] using Munsell samples of value 5/, compared each sample with a lightness scale and estimated the value of the neutral sample which appeared equally light. (According to theory, all Munsell samples of value 5/ should have equal lightness, namely 5/. This obviously was not found.) The locus of all the equal lightness values turned out to present a kind of hyperboloid in the CIE color space (as demonstrated by a beautiful perspective diagram). It seems that greatest discrepancies were found in the region of the "violet receptor." (Alas, people working in "applied physics" have no time to study Granit's dominator-modulator theory and cannot give up the outmoded idea that "violet"—or other—color receptors "contribute" to the "sensation of lightness." By now, they really should know better.)

That the problem of "lightness" is not that simple is, by the way, shown by further investigations of these authors.[94] The lightness of a given chromatic sample depends on background too, not only on luminous reflectance. Thus, the "lightness index" was found to be decreased when background and test patch were similar in color and increased when they were complementary. When the background was changed from black to white, all chromatic samples appeared less light with respect to a neutral scale.

The tricomponent theory of color vision is generally accepted as fact by the usual writer of college textbooks. By physicists it is usually believed in with intolerant

fervor, as the Ptolemaic system of the heavens had been by the church dignitaries of Galileo's time. That it is a theory at best, and that it is permissible not to believe in it, is not always conceded. It must have therefore been a pleasure to believers in the freedom of investigation to read a paper by Hurwitz and Jameson (to which short reference was made in my previous review) in which tetrachromatic stimulus curves were fitted to the known psychophysiologic data of color vision. But now, even for those who believe that the "pure" physiologic experiment has precedence even in matters of psychophysiology (and who so far have always rejected a tetrachromatic theory of color vision on the basis of the alleged experimental evidence of color matchings), there comes overwhelming evidence to support Hering's color theory in all its details in the epochal electrophysiologic studies of Svaetichin [95] on spectral response curves from single cones of fish. His experiments were carried out with 24 successive nearly monochromatic light pulses of different wavelengths between 40 and 750 mμ. He found that there are "three fundamentally different types of spectral response." The first type indicated increased intracellular negativity all through the spectrum, with a mean maximum response at 547 mμ and five submaxima. The curve was named L, since it seems to correspond with the luminosity mechanism (the white-black mechanism of Hering). The second type of response curve disclosed a depolarizing (negative) response to stimulation with shorter wavelengths, with a mean maximum value at 506 mμ, while on stimulation with longer wavelengths the electrical response underwent a polarity change, showing a hyperpolarization (positive) potential with a second maximum at 639 mμ. Svaetichin called this type of curve R-G, since nothing could fit better Hering's hypothetical red-green mechanism. The third type of response curve showed a hyperpolarization potential with a mean maximum at 460 mμ and a depolarization maximum at 610 mμ, perfectly fitting Hering's hypothetical yellow-blue mechanism, were it not for the fact that Hering originally assumed that the red and yellow mechanisms must be of similar "polarity" (he assumed both red and yellow to originate in "dissimilatory" changes of the respective visual substances), and this is certainly an insignificant difference. Svaetichin fittingly attached the name Y-B to this type of response curve. A neutral point appeared in both the R-G and the Y-B types of curve (in the former one at about 580 mμ) where the opposing components of the electric responses obviously cancelled each other. The anatomical substratum to these response mechanisms might, according to Svaetichin, be found in the peculiar arrangement of twin cones found in the fish retina, the twin cones being, at least in fish, "the peripheral mechanism for color vision, the chromo-receptors functioning in pairs in accordance with Hering's opponent color theory," while "the single type *L*-cone represents the retinal mechanism for the perception of luminosity."

In another paper, on the human photoreceptor mechanism, Svaetichin [96] writes that "considering that color vision has been found to be similar in all essential parts in both fish and man (4 maxima of the hue discrimination curve, a closed color circle, complementary colors), it can be said that all facts favoring Hering's opponent color theory also support the suggestion that the photoreceptor mechanism in both fish and human is built on the same general principles."

The limits of the field of vision for the perception of white were found to be normal by Schenk and Pfeifer [97] in patients with senile degeneration of the pigment epithelium of the retina. The field for yellow and blue was narrowed down. Dark adaptation showed a normal course. (This fact might aid in the differential diagnosis from genuine pigment degeneration.) (Although adherents of Hering's theory of color vision will be pleased with the authors' remark that

their results suggest the presence of special retinal elements which transmit the perception of yellow-blue, even they will hardly believe that such evidence bears very much weight.)

Maximum legibility depends on the contrast between printing ink and paper background. In combining colors (as now so often is found in advertising displays) care must be exercised, according to Hackman and Tinker,[98] to make a choice which provides for greatest brightness contrast. Two dark colors or two light colors should be avoided. Black on yellow or white, red on white, or green on red provide good legibility; black on purple, red on green, or orange on white are poorly legible.

Marriage between members of two families in each of which red-green blindness occurs cannot be as rare as Jablonski[99] assumes. Still, such pedigrees might be sufficiently interesting to warrant publication, especially if more information is given than this author found it worth while collecting. At the present state of our knowledge, testing with the Ishihara plates alone can not be considered adequate evidence anymore—especially not in the case of a seemingly color-deficient female, whose brothers, husband, and sons were found to be "green-blind." It is too bad that this pedigree was not given more expert analysis.

A good short and elementary introduction for the general practitioner to problems of color blindness was published by Ferguson.[100] It is regrettable that this type of popularization usually imparts to the uninitiated erroneous information, such as that protanopes are red-blind. Those who know better know, of course, that this is not the case, but this is no reason why the public, including the general practitioner, should be taught what is wrong.

Another good paper on faulty color discrimination, also on an introductory level, was published by Dvorine.[101] This author is known for his claims to have improved color vision. We feel reassured now to learn that "what success was attained with these individuals may have been due to the possibility that these color weak people learned to utilize other factors of discrimination," and, thus, another chapter of the eye-exercise quackery may, one hopes, have come to its well-deserved end by this honest admission.

Both of these papers are, of course, somewhat amateurish when compared with a report on diagnostic tests for color vision by Professor Wright,[102] of the Imperial College of London, a world authority on color measurements. Interestingly, Wright does not count the Hardy-Rand-Rittler test among the pseudoisochromatic plates, and he is, obviously, right, since this test is not based on any confusion of colors but on the confusion of a color with gray background. Even with its limitations, it is, according to Wright, the most promising of all confusion tests. The Farnsworth-Munsell test is also given due credit. One serious defect is that it does not provide for the abnormal spectral sensitivity of the protan observer. A keen protan observer might use lightness differences to arrange samples correctly or nearly correctly, even though his defect might be very marked. Lantern tests are important to establish a candidate's ability to undertake a job involving the recognition of color signals. They are of little value in diagnosing the type of defect. Much can be learned from this paper about the proper use of the anomaloscope and the spectral colorimeter. These instruments are, of course, beyond the reach of even the better-equipped medical centers, and only specialists will use them.

Wright's paper, abstracted in *Survey of Ophthalmology*, was commented upon by another color scientist, Walls, whose knowledge of the subject can hardly be called anything but formidable. The comments are no less informative and interesting than the paper itself, and if you are ready to build a home-made Nagel anomaloscope, better than the $1000 original, you find all the necessary specifications!

Those who can read German will find an excellent, simple, and easily understandable introduction to the use of the anomaloscope in a short paper by Monjé.[103] (It seems that the newer German instruments mix red lithium, 670, with green mercury, 546, while in the original Nagel instrument the green was thallium, 535. The yellow, of course, is sodium, 589.)

In an interesting paper Syng-Min Hong[104] discusses the much-neglected problem of acquired color vision defects. He classifies them into a retinal and a neural type. In the former the peak of the luminosity curve shifts toward red; in the latter it is unchanged. The range of the Rayleigh equation (expressing the relative amounts of red and green radiations which match a yellow one) is extended in both groups, since both suffer from color asthenopia. In the retinal group too much red and in the neural group too much green is needed for the match. In the neural group the relative subjective luminosities of mixed and monochromatic light agree with expectation, but this is not so in the retinal group.

To what amazing consequences mathematical statistics can lead in biology (and possibly other fields) one can see in a paper by Peters (a research psychologist) and Gross (a mathematical statistician)[105] to whom "Chi Square evaluations . . . surprisingly revealed that height was significantly associated with color blindness at the 5% level of confidence." Moreover, their psychological and statistical studies revealed another so-far entirely unexpected fact, namely, that "young adult males . . . are usually reluctant to admit that they are color blind."

IV. Ocular Refraction, Refractive Errors and Their Corrections, Visual Acuity, Optical Aids, Reading Problems

Sorsby and his team[106] produced an impressive study on "Emmetropia and its Aberrations." Correctly, they find that the existence of a greater number of emmetropes or near-emmetropes than can be expected on the basis of statistics is the central problem of the development of ocular refraction. They found in emmetropia a wide range of axial lengths, corneal powers, and lens powers (the respective values being 21 to 26 mm., 38 to 48 D., and 17 to 26 D.). There is a high correlation, however, between the first and the latter two, and so emmetropia is not the end-result of a haphazard combination. Ametropias up to ±4.0 D. are the result of faulty correlation of, in themselves, normal components. Lens power is highly correlated with axial length regardless of refraction anomalies. The correlation between axial length and corneal power is the expression of the circumstance that in longer eyes corneas are flatter. The term "combination ametropia" introduced by Tron is an unhappy one, since emmetropia too is the result of combination. High ametropia is axial in origin (the length values are usually outside the normal range). Observations on children between 7 and 16 years of age indicate increase of axial length at the rate of 0.2 to 0.3 mm. per year. The excess of high myopes over high hyperopes is, in part, apparent only, since (to give two examples) the spectacle refractions of −20.0 and +13.5 D. represent axial errors of the same order and −30.0 D. spectacle refraction corresponds to only −21.9 D. of myopia.

In a paper on the "Genesis of Myopia" Professor Otsuka,[107] chief of the department of Ophthalmology of Tokyo Medical and Dental University, presents the résumé of some 30 papers published by him and his collaborators in Japanese medical journals since 1843. His views conflict to a certain extent with opinions of T. Sato, another distinguished Japanese author, according to whom myopia is mainly caused by an increase of the refracting power of the lens. Their controversy is little known in this country, and it is hoped that this review draws some attention to it. Otsuka bases his theory on a study of 1180 eyes of 295 sets of twins and concludes that both the ocular axis and the lens participate in the genesis of

myopia. The normal elongation of the ocular axis after birth by 8 mm. should cause a myopia of 30 to 40 D., were it not for the flattening of the cornea, the deepening of the anterior chamber, and, mainly, for the physiologic changes in the refractive power of the lens. These latter changes have two components, viz., the flattening of the curvature of the front surface of the lens and the decrease of the difference in refractive index between nucleus and cortex. It is not quite clear to me whether Otsuka blames close work during the growing years as one of the causes of myopia. He thinks that both the elongation of the axis of the eye and the failure of the adaptive decrease of lens curvature participate in the genesis of myopia.

A very fine paper by Nadell, Weymouth, and Hirsch [108] discusses the various pitfalls in past and present statistical studies on so-called school myopia. Analysis of their own data fails to reveal any relationship between the amount of reading done and the distribution of the refractive state.

Weekers and associates [109] studied 14 pairs of homozygotic and an equal number of heterozygotic twins. In 13 pairs of the former, hypermetropia and astigmatism were almost identical (with the arithmetic mean of differences at 0.9 D.). In 13 pairs of heterozygotic twins the mean difference of hypermetropia and astigmatism was 3.2 D. The remaining pair of monozygotes had myopic astigmatism. This pair was, possibly, prematurely born, and their myopia might have been the outcome of prematurity rather than of generic nature. The astigmatism of the twins was nearly identical, while the myopia of one sibling was 5 and 13 D. greater than that of the other. Of the last pair of heterozygotes one sibling was mildly hyperopic and the other was a high myope, and the astigmatism of the latter was about three times that of the other. (Unfortunately, the authors have not stated whether the given values refer to the *real* refraction and astigmatism or the corrective lens. In high myopia the two are rather different, and this very important material could have been even more useful and informative if, instead of [or besides] the values of astigmatism, the keratometer readings would rather have been furnished.)

A valuable study by Gregory [110] concerns itself with the examination of 30 children known to have had retrolental fibroplasia but possessing some residual vision. In 85% of them myopia varying between 2.5 and 18 D. was found in at least one eye. This congenital axial myopia with albinism of the eyeground is obviously in some way correlated with prematurity, and the author suggests that, in general, prematurity might be one of the factors in the causation of myopia. The visual function of these myopic eyes was actually less disturbed than that of the hypermetropic fellow eyes, the development of which was often reminiscent of microphthalmos.

Myopia, according to Kosinski,[111] is a symptom of a general weakness of the connective tissue, which also manifests itself in inguinal hernias, varicose veins, etc. In school myopia this weakness of the mesenchyma manifests itself in the eye. Reading is the "military march" of the eyes; the sweep from the end of one line to the beginning of the next causes "waves of congestion and pressure" which are analogous to the syndrome of varicosity, and affect the posterior pole of the eye. "To conquer therapeutic nihilism . . . the well-tried drugs of the homeopathic-phytotherapeutic treasury of medicines are given to treat the causal weakness of the mesenchyma." Equisetum, Aletris, Calc. fluor., Adonis, Melisse, Glycocoll, Prolin, L-ascorbic acid, Hamamelis (space forbids enumeration of them all) is made up into Bulboton eyedrops and tablets. How much this helped, alas, no statistics reveal. No controls are mentioned.

(Kosinski is, by the way, the same author who discovered that senile cataract is related to gallstones and should better be called cataracta hepatica and whose "Sulfolithon" dragées offer a cure for both, gallstones and

cataract, not to mention such triflings as vitreous opacities and chorioretinitis.)

(And since we are digressing toward therapeusis, of which, alas, so little is contained in this review, I might mention that the back cover of almost every issue of the venerable *Klinische Monatsblätter für Augenheilkunde* carries a full-page advertisement of Augentonicum-Sculln, an eye preparation containing digitalis. Of this a respectable source, Hollwich,[112] from Thiel's clinic, reports that it affects favorably the "nervous" asthenopia of the young and the "muscular" asthenopia of the older, while another author, Nieminen (1956), even found after its use a "decrease of the angle of squint" and "entire disappearance of headaches." One ought to try it.)

The interesting case of a physician who, in order to lose weight, took three tablets of acetazolamide (Diamox) and developed transitory monocular diplopia and myopia is described by Schirmer.[113] The author reminds us that monocular diplopia and myopia have been repeatedly described in connection with the intake of sulfonamides, a group of drugs to which acetazolamide also belongs.

Kronning[114] describes two cases of transient myopia after the use of acetazolamide. The first, a woman, took it for edema of the legs in pregnancy; the second, also a woman, took it for reducing purposes. In her case the depth of the anterior chamber was found considerably reduced (which could well account for the myopia) and the amplitude of accommodation was diminished. In both cases the original refraction returned after cessation of medication.

(I find that I missed reporting on a case from the literature of 1956, the case of M. Back [Transient Myopia After the Use of Acetazoleamide, A. M. A. ARCH. OPHTH. 55:546-547, 1956], in which a man taking acetazolamide for reducing purposes had been described.)

Pénzes[115] describes a case of transient myopia of 3.5 and 2.5 D., respectively, in a young woman suffering from acute gastritis. He gave atropine eyedrops, believing that the myopia was caused by a spasm of accommodation, but this did not change the refractive error. It subsided all by itself within three or four days.

An editorial by Hirsch[116] on visual acuity deserves respectful attention, like any publication of this eminent author. He does well in destroying the much-propagandized illusion that visual acuity when determined with both eyes open (as is done with the commercially available "sight-screening" instruments) is measured under more "natural" conditions than otherwise. The subject tested with these instruments is expected to fuse two objects peripherally and to identify a test pattern simultaneously with one eye. The central area of the other eye must at the same time "suppress or at least ignore," which is certainly not a natural situation. Viewing the usual Snellen-type target with one eye while the other is occluded is actually a more natural situation, encountered every time one closes one eye. The clinical value of the usual visual acuity tests rests not upon simplicity or naturalness but upon the fact of accumulated clinical experience over the years which established this measure as a standard.

(To this, Slaton,[117] in a letter to the editor, remarks that the fact that a person sees 20/20 with one eye when the other is occluded does not mean that he actually sees 20/20 with that eye when both are open. It might be 1.00 D. more hyperopic and not accommodated sharply upon some target fixated by the other eye.)

Another publication by Hirsch[118] deserves attention as an example of how a statistical study on ocular refraction and the influence of some extraneous factor upon it should be set up. The paper deals with the relationship between measles and myopia and suggests, at least in a preliminary fashion, that such a relationship does in fact exist.

Femmer,[119] a German physician and government councilor, discusses the question of whether, under German law, determina-

tion of visual acuity by opticians is permissible. He found that among 2000 persons coming for eye examination because of failing vision 1694 had no ocular pathology while in 306 medical diagnosis and treatment were indicated. I quote from his English summary: "4. The test for eyeglasses in a case of presbyopia means not only the physical-technical refraction; then serious and even dangerous diseases could be overlooked which would require urgent treatment. The testing for eyeglasses is therefore a medical procedure. 5. Inadequate vision is in ophthalmology the most frequent symptom that brings the patient to the doctor. Whether the cause for this lies only in an error of refraction or a serious disease underlies . . . can only be assessed after detailed examination of the eye."

Zanen and Klasssen-Nenquin [120] published a good short résumé of newer literature on the relationship of visual acuity to exposure time, adding studies of their own with instrumentation previously (1952) described and recently improved. They use chessboard targets and find that the relationship can be expressed by an S-shaped curve, visual acuity decreasing to about "0.6" when exposure time drops to 1/500 second. They confirmed a previous finding of Ehlers (1948) that in strabismic amblyopia "visual velocity" is good in spite of poor visual acuity while it is poor when disturbances of the media, the retina, or the optic nerve are the cause of reduced vision.

From Leverett's [121] statistical study on the vision test performance of some 6000 elementary- and secondary-school children one learns that the proportion of children who fail the visual acuity test increases from the 1st to the 12th grade. (This, of course, has been known for nearly 100 years. Some children will become myopic who in the beginning passed the test.) The proportion of children who fail the plus lens test increases slightly in the first and second grades. The percentage of children who fail one or more phoria tests increases constantly from kindergarten to 12th grade, "reflecting, in all probability, an increasing frequency of acquired motor anomalies."

One hundred children in the fifth and sixth grades of a suburban school were screened by Steinbaum and Kurk [122] both with the Snellen chart and with the Keystone battery of tests. A comparison of the results with one of the tests (costing approximately $1.00) and the other (costing $150.00) shows that the correlation was fairly good. With use of the rigorous criterion of 20/20 vision or perfect scoring, respectively, 48% failed with the chart; 66%, with the battery test. Even with a less rigorous criterion, 20/30 vision or a score of 88 or better (out of a possible 100), 22% and 33% failed, respectively. One cannot help but feel that the battery test not only is more expensive, and not only needs trained personnel for its administration, but also results in an unrealistic number of failures, with the heaping of unnecessary referrals. (I believe, of course, that every child should be seen by an *ophthalmologist* before the age of 5, but that is another matter.)

Donabedian and Rosenfeld [123] examined the "replicability" of the Massachusetts screening test. In young children they found it very low. "Whatever may be the reasons which cause variation in results, it seems evident that a simple test of visual acuity does not give results that are sufficiently reliable for effective screening among young children."

Several papers have in recent years appeared on so-called maintained, or stopped, vision. This is an artificial condition in which the retina is prevented from receiving its normal form of stimulation as the effects of the usual incessant motions of the eye are neutralized (see last year's issue of this review). Riggs and his associates (1953) found, e. g., that the usual acuity for a dark hairline decreased rapidly in the absence of retinal image motion (except when exposures were very short). Krauskopf [124] studied the contrast sensitivity under a new, even if related, set of condi-

tions, offering a brilliant refinement of technique in which the actual retinal image motion was eliminated by a contact lens arrangement but controlled motion of image of various frequencies was introduced instead. He found that low-frequency vibrations of 1 to 5 cps and at least one minute amplitude were beneficial for vision while high-frequency vibrations of 10 to 50 cps were detrimental. It seems, then, that not all the different types of retinal flicks, drifts, and jerks are essential for good retinal resolution but only the larger ones of smaller frequency, while the fine fixation tremor of 100 cps and 20-second amplitude has little effect.

Sédan, Jayle, and Farnarier [125] compared the monocular and binocular visual acuity, using Landolt and Márquez rings and Monoyer letters, in ametropes, emmetropes, and anisometropes. In the latter group the degree of improvement is more marked when binocular vision is present. Furthermore, improvement of binocular visual acuity is greater when the monocular visual acuities are relatively low and when they are different. The improvement is small in emmetropia. There are several hypotheses to explain the superiority of binocular over monocular vision. These were critically sifted, and the authors favor the hypothesis that central summation and interaction between the two eyes are the main cause of improvement. Whenever one eye is separately tested, the shapeless impressions from the covered eye hamper best vision. The authors discuss much of the pertinent literature, but there are no references.

Lewinski [126] studied several methods of determining visual acuity objectively using a chessboard pattern. (All are based on using the optokinetic nystagmus as the indicator of retinal resolution and the smallest angular size of a chessboard square which still is able to elicit ocular movements is the measure of visual acuity.) In 6.1% of his cases objective visual acuity appeared to be better than the visual acuity determined by subjective methods, while in 9.3% it was found to be worse than the latter. In the rest of the cases, the two methods gave reasonably similar values. The author also reports on a new type of stimulus pattern which obviates the technical difficulty of producing chessboard patterns of sufficiently small angular extent. The minimum angle of resolution with this technique was found to be in the neighborhood of 30 seconds of arc.

With the collaboration of Zeiss, Jena, Günther and associates [127] constructed a new instrument, the "nystagmovisometer," for determining objective visual acuity. Some 200 eyes were tested with this instrument, with visual acuities between 0.01 and 1.7. Average errors amounted to 7% to 10%. Myopic eyes were found to resolve the chessboard pattern better than usual optotypes.

Sachsenweger [128] describes a projection instrument with which both subjective and objective visual acuity are easily measured. Subjective visual acuity is determined by projecting a Snellen chart. For the objective determination of visual acuity he uses slides with chessboard patterns and an electric motor with an excenter to shift the slides in a to-and-fro manner. Both the frequency and the amplitude of the pendular nystagmus elicited by this motion can be regulated. The advantages of such an instrument are manifold, since it makes it possible to determine visual acuity with both methods under uniform and standardized conditions (equal illumination, equal adaptation, equal test distance, contrast, etc.).

Gorman, Cogan, and Gellis [129] built an instrument to determine visual acuity, objectively, in infants 1 to 5 days old. The regular optokinetic drum gave very inconstant results. Their very ingenious instrument consists of a 16 ft. long scroll of white paper across the width of which black lines are printed. There are two sections. In the first the width of black lines and white intervals is 0.05 cm.; in the second, 0.15 cm. A positive response could be elicited in 90% of the infants examined. (The distance from the infants' eyes was kept at about

15 cm.; the speed of rotation of the striped paper was about 2.3 cm. per second.)

There is at least some indirect evidence, according to Griffith,[130] that television viewing affects children's vision. He found a significant increase in the percentage of children over 11 years of age who wore correction for myopia in families that had television sets as compared with those in families that owned none. (As to his appraisal of television, "The programmes may stimulate thought, improve appreciation of the arts, extend knowledge of literature, and produce better understanding of social problems, but they may also encourage a child to depend on ready-made entertainment, dampen initiative, discourage rational reasoning, and decrease his readiness to accept responsibilities. The youth club which the child may otherwise be attending might have fostered his social and emotional development better than the television."—a typically British understatement about the detrimental effects of one of the "blessings" of our civilization.)

(Griffith's paper, by the way, prompted a number of letters to the editor of the *British Medical Journal*. None of them would agree with his conclusion and, in fact, his statistical evidence is poor indeed. The fight against the pernicious television-habit will have to be fought on other than ophthalmologic grounds.)

A most welcome critical review of what little is known about monocular diplopia was published by Gramberg-Danielsen.[131] Cases can be classified according to the literature into several groups. Monocular diplopia can be caused (1) by primarily physical disturbances (of cornea, anterior chamber, iris, and especially the lens); (2) by "nerval" (certainly a more cautious term than "nervous") or innervational disturbances which secondarily affect the optic apparatus (e. g., astigmatic accommodation); (3) by parafoveal fixation (e. g., following stabismus surgery or in homonymous hemianopia), and (4) by cerebral disturbances. The author is rightly critical of those who lightly characterize monocular diplopia as "hysterical" and believes that in cases belonging to Group 4 ocular motor innervation is at fault. Thus these cases actually belong in Group 3. He does not believe in cerebrally induced monocular double vision.

A comprehensive survey on visual problems in industry, in three parts, was published by Fry.[132] Some of the topics discussed are requirements for efficient seeing, the role of the visual experts in industry, providing light for jobs that require primarily central vision (including direction of lighting, differential lighting of objects and background, wavelength composition, quantity of illumination, etc.), the effect of the surroundings upon the performance of a task requiring central vision, providing light for jobs which require peripheral as well as central vision, jobs performed at low levels of illumination, relation of refractive errors to performance, fixation and convergence, seeing with comfort, visual fatigue, and finally, seeing with safety—quite an array of subjects.

Guerry[133] deplores the lack of visual standard requirements for the issuance of driver's licenses in the various states and territories. He feels that the first step to rectify this deplorable situation should be the setting up of a board of opthalmologists with members chosen from the principal ophthalmological associations. He finds that "a few states have recently taken a great step forward in the screening of driver candidates by employing one of the various screening devices." He reports that persons disqualified by such screening are referred to a physician for medical attention (seemingly forgetting the interest revealed and the pressure applied by certain groups for both the installation of these commercially available but fully unnecessary devices and the channeling to *their* members of those disqualified by these devices). He wants repeat offenders (or drivers who have had several accidents) retested by a screening device and those who show visual defects

referred to a state evaluation board for more complete study (which is certainly a good suggestion). Persons with visual defects that cannot be reasonably corrected should be either prohibited from driving or be allowed to drive only under definite restrictions.

Ophthalmologists who are interested (all should be interested) in classroom illumination and need an elementary introduction will find this, and some good points, in a paper by Francis.[134]

An excellent paper from the U. S. A. F. School of Aviation Medicine, by Gerathewohl,[135] deals with the conspicousness of flashing light signals. Three brightness contrasts (0.16, 0.95, and 11.16), three frequencies (one flash every three seconds, one every second, and three flashes per second) and two flash durations (0.1 and 0.2 seconds) were tried. The effect of the duration could not be clarified, but, of the other two conditions tested, one flash three times per second and at least twice as bright as the background was found to be the most conspicuous.

A paper from the Lamp Division of the General Electric Company, by Guth,[136] once more proves the long-known fact that "older workers require considerably higher levels of illumination in order to achieve a given ability to see." While Weston, the British expert, came to the melancholy conclusion that "even with the highest illumination the older group was unable to achieve the same performance as the younger group did with the lowest illumination," our author reassures us that "older workers can be expected to achieve the same visual abilities as younger workers" provided they use more light. (We older ones can thus sigh with relief.)

One of the subjects which only my duty as reviewer makes me reluctantly cover, but for which I never could whip up actual interest, is the problem of glare. It was for this reason mostly, not having any personal opinion in the matter, that I felt compelled to restrict myself so far to noncommital reporting (or none at all) of papers on this subject. Another of these papers, by Fugate,[137] I would have again left unmentioned (or at least without comment) were it not that O. Lowenstein, certainly our greatest authority on the actions and reactions of the pupil, in his comment (Survey Ophth. 2:331, 1957) on a previous paper of this author, remarks that "some of the conclusions are entirely unfounded" and that "this work was not guided by thorough knowledge of the anatomy and physiology of the iris and its nervous control." We can, thus, dismiss a discussion of speculations on the mechanism of "discomfort glare" until better evidence is at hand, without feeling too great a guilt for this sin of omission.

A short introduction into the practice of refraction by Gettes [138] should be a welcome addition to the bookshelf, especially of the beginner. It is a good book, and even persons experienced in refraction (especially if their job is teaching younger colleagues) will learn a lot from perusing it. The arrangement of the material is unusual. For one who did not grow up in Boston, the author devotes an unexpectedly large number of pages to subjective methods, especially the astigmatic dial. (And this is gratifying.) It is also pleasing to see a separate chapter on "Aids for Subnormal Vision" included. (One grave but common error cannot be left unmentioned. Figure 38 on page 99 shows parallel rays made convergent by the hyperopic eye, toward a point behind the retina marked *p. r.*, obviously for punctum remotum. That point is the second principal focus of the hyperopic eye. The punctum remotum is another point.)

Eggers [139] describes an interesting method by which to estimate the approximate status of refraction. He observes the fundus reflex in the pupillary area from a distance of about 12 in. and notes the darker and lighter areas seemingly located in the pupil. Their relative position and extent varies with the state of ocular refraction. The described phenomena are caused by the construction

of the modern electric ophthalmoscope, in which the sight hole is displaced relative to the axis of illumination. Thus, not all reflected rays can pass through the subject's pupil and the hole in the ophthalmoscope. This leaves part of the pupil apparently less illuminated. The area varies with myopia and hyperopia. Both of them and astigmatism can be estimated by this appearance, and with considerable accuracy.

The interest in the Rodenstock refractometer has not shown any great increase, and it is still hard to judge its place in the "armamentarium of the busy ophthalmologist." In fact, Volk,[140] in a letter to the editor of the *American Journal of Ophthalmology* questions even the limited usefulness Hobbs and Schimek have ascribed to it in their paper analyzed in last year's edition of this review. Hobbs and Schimek, while assigning to it "some values during a routine refraction . . . personally do not believe the place of the present Rodenstock model will be prominent in office practice. Nor do we think it should replace retinoscopy."

"Ophthalmometer" was the name given by Helmholtz to an instrument with which measurements on the mirror images of the cornea and lens could be carried out, and also all kinds of other measurements relating to the schematic eye or to optical images. Siebeck,[141] in a historical note, emphasizes that this instrument was rightly called ophthalmometer, while it is unjustified to use the name for the keratometer of Javal and Schiøtz or for any other instrument which only measures the corneal meridians and radii.

Raubitschek,[142] the well-known originator of a beautiful test for the determination of astigmatism (it was named Ioskiaskopy by Pascal in his English report on the method), describes a modification of an instrument now called the "Pascal-Raubitschek test for astigmatism," to the perfection of which the late Dr. Pascal devoted much of his last efforts. The basic design of Raubitschek's "arrow" dial has been retained; the scale for plus-cylinders has been eliminated. When the use of this dial is combined with the use of another rather new (and in this country still not too well known) instrument, the variable cross cylinder (called "Astikorrekt") of Siebeck (1954), both the axis and the power of ocular astigmatism can be determined within minutes.

While many of us routinely use Jackson's cross cylinder, (and would not know how to refract without it), we have just taken some annoying side-effects during its clinical application for granted. We should be grateful to Haynes [143] for an interesting and elucidating mathematical analysis of the so-called scissors effect. This analysis shows that the 0.5 D. cross cylinder offers a certain amount of intrinsic magnification along its plus-power meridian and similar minification along the minus-power meridian and that the rotary deviation or scissors effect caused by this differential magnification is greatest along the 45- and 135-degree meridians. This effect can be eliminated for one position of the cylinder by choosing a suitable front curve (this influences the so-called shape factor of the magnification) but the beneficial image-equalizing effect comes to nought when the cross cylinder is "flipped." Thus, actually two cross cylinders are needed to have the full effect. (How Haynes' double cross cylinder, once it becomes commercially available, will work in practice will be awaited with interest. By the way, why Haynes uses the awkward and incorrect term "homokonic," when everybody would understand the correct term "iseikonic," I cannot understand.)

Bonnet [144] gives an excellent short introduction to the optical theory of contact lenses. He explains (with the help of a minimum of simplified formulas) the choice of powers and curvatures and the influence of contact lenses on image size and accommodation. He thinks that in unilateral aphakia corrected with contact lens the wearing of an iseikonic lens of about 8% magnification is advisable. (I have usually not found this necessary.)

An editorial by Rudolph [145] in the *Transactions of the American Academy of Ophthalmology and Otolaryngology* deals with the activities of the committee organized by the American Standards Association to arrange for suitable standards for spectacle lenses. "We intend to make them as high as the best of minds and machinery can produce without inflicting a prohibitive price upon the consumer." The committee has a "keen interest" in surface and physical characteristics of glass, tints of glass, plastics, tolerances in prismatic effect, cylinder axis, power, centration, and thickness. The 1950 meeting of the Association of Independent Optical Wholesalers recommended the exclusion of all but corrected curve lenses from the market, which, obviously, would increase prices unnecessarily, and the author agrees with Lebensohn that "corrected curve lenses are essential in plus compounds, but in single spherical lenses, plus or minus, and in compound minus lenses there is no essential difference between the toric and corrected curve conflexures."

A report of the Committee on Research and Standards of the American Optometric Association [146] on "Surface and Glass Defects in Ophthalmic Lenses" is of obviously little interest to the average ophthalmologist. Those who might be interested will in this report find a short nontechnical description of the usual flaws of ophthalmic lenses and of the tests for their detection. Excellent photographs and some good drawings illustrate the flaws as they appear during these tests.

Ophthalmologists seldom will even read material referring to lens manufacturing processes. Even less often will an ophthalmologist be sufficiently expert to write on the subject. A welcome exception is Keeny,[147] who devotes a short but excellent monograph to a study of lens materials from the point of view of preventing ocular injuries. Anyone interested in the subject (and one must be interested in it) will learn all it is necessary to learn from this little booklet about glass and plastic materials used as ophthalmic lenses, their properties, and their indications and contraindications.

Davis,[148] of the Research Department of the American Optical Company, has put an amazing amount of work into the analysis of the optics of plano lenses, extensively used in sunglasses or safety devices. After perusal of the voluminous data I feel reassured that the eyes are very well able to take care of the distortion, magnification, prismatic effect, etc., especially since the two eyes are usually affected in a similar manner. When a plano lens is prescribed for one eye and a correcting lens, for the other eye, the problem is a different one, and there the optical properties of the plano lens must be considered as well as those of the other.

The demands for vision have changed in the nearly 100 years since Donders published his great classic on the anomalies of refraction and accommodation. Glasses should, according to Schober,[149] nowadays be prescribed with main emphasis on working vision, and job selection should not be based on distance visual acuity alone. Prescription of working glasses for near vision on the basis of test types alone is "careless and irresponsible." Near phorias and the accommodation-convergence relationship must be studied and binocular balance achieved. Two new German vision testing instruments are described (one of them an improved copy of the British Freeman Near Vision Unit). The author thinks that the use of such instruments is a must (and, since I have been using the Freeman instrument now continually for about two years, I can heartily agree).

Much can be learned about the management of anisometropia from a paper by Lebensohn.[150] In 200 consecutive cases in which the power difference in the vertical meridian was 0.75 D. or more, he found hyperphoria of 0.5△ or more in 80% and of 1△ or more in 50%, and he believes that the principal cause of discomfort in anisometropia is due to heterophoria, especially

induced hyperphoria when looking down. The latter, however, should not be corrected without first considering the influence of any intrinsic hyperphoria and anisophoria that might be present for distance or near and which, according to the studies carried out by this author some years ago, simplifies rather than complicates the handling of this problem in two out of three cases. In the relevant measurements of hyperphoria with the Maddox rod it is important to ascertain which is the fixing eye, as the author found differences with changing fixation in 55 of his cases. Data with the dominant eye fixating should preferably be used. (He advises testing without eyeglasses and with the dominant eye fixating the light for both distance and near, while the Maddox rod should be placed in front of the nondominant eye.) Illustrations used show when to use the slab off method, when to use different types of bifocals, or even when to use a bifocal for one eye only. In case of high anisometropic myopia, he finds it often wise to abandon the attempt to secure binocular vision, adapting one eye for distance and the other for near use. He finds contact lenses an excellent and sometimes the only solution in monocular aphakia and monocular high myopia. Supplementary spectacles usually add to their visual effectiveness.

Cornell University Medical College devoted one of its Conferences on Therapy to "Eyeglasses as a Therapeutic Agent." The discussion was opened by McLean.[151] It is worth reading. One will not learn anything about optics or refraction but will have the pleasure to listen to the ideas of an outstanding clinician on a great many topics, such as sunglasses, contact lenses, and the use of glasses for the treatment of extraocular muscle imbalance. He believes that the pediatrician should examine the eyes of the newborn "externally and ophthalmoscopically the very first time he examines the newborn baby." He thinks that very few headaches are caused by uncorrected refractive error; he has not much use for the correction of aniseikonia. He is against putting myopic children into "sight-conservation" classes "in spite of the fact that there is no evidence that these classes conserve anything." He does "not believe that there is any sound evidence that any organic harm will come to eyes either from wearing or not wearing glasses because of refractive errors."

The long-awaited report on the effect of tachistoscopic training on visual functions in myopic patients by Berens, Girard, Fonda, and Sells[152] (the latter is an expert, I am told, in medical statistics) has finally appeared, and it is as fine a piece of research as could be done with the type of material available and under the given restrictive conditions. It seems that those of us who so far were convinced of the utter usefulness of eye exercises for myopia and questioned the integrity of those who did give such exercises will at least have to qualify our objections, as those myopes who went through a training course according to the well-known (it seems I was gravely unfair when on one occasion I called it notorious) Renshaw training procedure showed increase of visual acuity, form field, and reading speed. The average improvement of the refractive condition of the eye was, of course, minimal: 0.22 D.

The controversial issue of the "effects of visual training on visual functions" was also reviewed by Sells and Fixott.[153] "Learning to interpret a blur" is the most generally acceptable explanation of the type of improvement reported in the previous paper, but, as the authors correctly emphasize, this should not be interpreted as "depreciation of the significance of such learning." They quote, at length, several of the unforgettable passages of Lancaster's de Schweinitz lecture (1944), and their conclusion is that "one phase of the visual performance is trainable . . . . The improvement of many aspects of visual performance through perceptual learning is a fact."

Elementary clinical geometric optics seems to be a kind of dead science in which there

is hardly any new development ever expected. Still, there is news, sometimes even surprising news. It is, for example, assumed to be a general rule that convex lenses lose efficiency when brought closer to the eye, and not much thought is ever given to the validity of this assumption. Recently Lindner has pointed out that this is only a rule of thumb and not generally valid for the corrected hypermetropic presbyope. In fact, he showed that the rule changes into its opposite when the reading addition is stronger than the distance component of the lens. And in an interesting and easily understandable short mathematical essay, Graff [154] proves that the rule is also not valid whenever an object of regard is brought sufficiently close to the accommodating hyperopic eye corrected for distance. In fact, the calculations show that a convex lens of a certain power has to be replaced by a weaker one in case the lens is displaced toward the eye in all those instances in which the reciprocal object distance (measured in diopters from the correcting lens) is greater than one-half of the vertex power of the correcting lens.

Calculation of refractive corrections in their dependence on the distance between eye and glasses is one of the favorite pastimes of ophthalmic opticists. It has been taken up once more by Roelofs.[155] Real refraction R (at the anterior principal plane of the eye) can be determined from the formula

$$R = \frac{L}{1 - \frac{Ld}{100}}$$

where L is the correcting lens and d, the distance between lens and the principal point. The *real* astigmatism (the difference between the real refractions) $R_1 - R_2$ is found after both values have first been determined according to the above formula. "Suppose with a trial frame where d = 2.5 cm. we find good correction with sph. −21.5 and cyl. −5.0. The real refraction is 14.0 sph. with −2.0 astigmatism." (An extreme example, obviously, serving a didactic purpose, for who will ever use a trial frame at $d = 2.5$ cm.!) Very interesting (and to those not aware of the work of the late Pascal, even astounding) are Roelofs' calculations regarding the discrepancies in actual accommodative performance as the power and position of the correcting lens are changed. Seldom does one realize how much *actual* accommodation can differ from apparent accommodation when the corrected refractive error is of greater than moderate degree.

J. Barraquer,[156] of Barcelona, the author whose enthusiastic report on the treatment of myopia by scleral shortening I reviewed last year with reluctant admiration and much scepticism, has now turned to the operative treatment of refractive errors with plastic lenses introduced into the anterior chamber. His indications are (besides aphakia, of course) nonprogressive high myopia and high hyperopia in one eye (to correct anisometropia) or in both eyes (to increase visual efficiency). Of the 62 patients operated on 28 were such refraction cases. He never has had any serious complications, and if he miscalculates the dioptric power of the lens he does not mind (neither, seemingly, do his patients) substituting one lens for another.

Our American surgeons seem to be more cautious and, as far as I am aware, only two reports are at hand, one by King and Skeehan,[157] who performed the implantation of a Strampelli lens in three cats and three monkeys, and another by Lieb and Guerry,[158] who report on their very favorable results on eight humans. According to the first two authors, the insertion produced only minimal irritation. Only in one cat eye was there some complication, but that was rather due to the operative procedure than to the plastic material. The report by the latter two authors is interesting and very encouraging. An important feature of their paper is a table in which conventional lens power 12 mm. from the cornea is translated into equivalent powers of the proper anterior chamber lens.

Reese and Hamdi [159] reported on five years' experience with the Ridley opera-

tion. Thirty-nine per cent of their cases have 6/21 or better vision without glasses; seventy-four per cent have vision of 6/12 or better with correction, and sixty-four per cent have vision of 6/9 or better with correction. Sixty per cent of their cases see Jaeger 3 or better with correction. Most patients read fairly well even without glasses. These authors are very enthusiastic about the Ridley operation. "If it, or any of its modifications, prove feasible and practicable—and we believe they will—its benefits can hardly be calculated."

The more conservative of us take heart in the meantime from Goar's [160] statement that "it seems more sensible to place the foreign body outside the eye." This author had so far collected 63 cases of monocular aphakia corrected with corneal contact lenses and finds the results most gratifying. "The degree of fusion does not seem to matter much. Some obtain primary fusion only. Many acquire third degree fusion." He concludes that "the advantages of this method of treating persons with monocular aphakia far outweigh the disadvantages."

A case of monocular aphakia successfully corrected with a contact lens (Lacri lens) is reported by Levitt.[161] The case is certainly worth reporting, since the patient was only 7 years old. He learned to insert and remove the lens and has been wearing it from "arising to retiring" without complaint.

Thomas [162] thinks that it is safe to fit contact lenses to aphakic patients about six months after surgery.

Strampelli's anterior chamber lens has caught the fancy not only of the surgeon but also of the lens designer. We learn from the calculations of Emmrich [163] that its refractive power in air is 48.506 D.; its thickness, 1.0 mm., and its anterior and posterior radii, 12 and 63.748 mm., respectively. In the anterior chamber its refractive power decreases to 15.43 D. The aphakic eye has a refraction of 43.05 D., and the Strampelli lens, placed at the theroretical distance of 2.05 mm. behind the cornea, increases its power to 57.40 D., which is still about 1.0 D. less than the power of the schematic eye of Gullstrand (58.64 D.).

A short discussion of the optics of visual aids with remarks about the usefulness of the different types was published by Horowitz.[164] (I mention this paper less for any new material it would contain but because it is, as far as I am aware, the first one in the European literature to deal with the newer, mostly English and American, developments in this field.)

Gordon and Ritter [165] (who, working at The American Foundation for the Blind, have probably the greatest experience in the field) published a paper on low-vision aids meant for general practitioners. Even if not interested in the actual fitting, they *should* know of this new development and be able to advise their patients accordingly. (Anyone in need of a nontechnical introduction into the subject will read this paper to his best advantage, but even the experienced will find in it some pearls of wisdom—and wisdom as much as knowledge is, indeed, necessary if low-vision aids are to be prescribed successfully.)

The dioptric power of the magnifier required by a given patient with reduced vision is determined, according to Sloan and Habel,[166] by (*a*) the remaining visual acuity and (*b*) the near point of distinct vision. They describe a test for the determination of near visual acuity in cases of reduced vision. This test gives sufficient information as to the required magnification of the retinal image for useful reading vision. (To determine accommodation in a case of subnormal vision is in itself a problem not yet fully solved.)

A system of equations developed by Westheimer [167] deals with the useful field of visual aids. His calculations show that the size of the pupil has little influence upon the extent of this field. On the other hand, it turns out that the field of the stationary eye is greater than that of the moving eye, explaining the seemingly strange phenomenon that objects one can see through one's glasses in peripheral vision are no longer

visible when the eye is turned to look at them. In the simple case of the hand magnifier with the object at its focal plane, the span visible to the moving eye is directly proportional to the lens diameter and indirectly proportional to its distance from the eye and its power. In the case of objects at infinity the span of vision depends not only on the position of the magnifying lens but also on its power, and strong plus lenses limit the field. In telescopic systems both the aperture of the objective (plus) lens and the magnification influence the span of vision, the latter in an inverse manner.

A new type of step (one the possible significance of which might be even greater than is at first apparent) in the direction of helping the partially sighted was taken by Prince.[168] He found that many who with uncorrected subnormal vision could not read some conventionally spaced print, could read the same print if it was more widely spaced. "Scientifically planned inter-letter spacing might thus even help people with uncorrectable subnormal vision." Prince intends to extend his studies in this direction, and his results will be eagerly awaited.

It is welcome that finally someone has written about the usefulness of contact lenses as visual aids in subnormal vision. Most of us who have written about the subject have so far neglected even to mention them. Williams,[169] in a new semiscientific magazine, *Contacto*, calls our attention to them and gives a good elementary discussion with many practical hints.

Anyone interested in the education of partially sighted children will read with pleasure and much benefit the transcript of a conference arranged by the National Society for the Prevention of Blindness.[170] Besides teachers, some adept and intelligent high school students participated in this conference. Relating their experiences in sight conservation classes, they made excellent suggestions for the improvement of such classes.

Schillinger[171] gives valuable suggestions to surgeons who by the time they become successful usually also reach the age of presbyopia. He describes the various surgical visual aids available, weighing the advantages against the disadvantages of each type.

A short report of Jaensch[172] advises about the passing of the first law in one of the German Federal Republics (Baden-Württemberg) about special schools for children with poor vision. The law makes school attendance compulsory even for the defective child. At the same time, it makes it the duty of the state to provide special classes (even boarding schools) starting from preschool age. Vocational training up to 20 years of age also becomes compulsory.

Jaensch[173] reports about 206 one-eyed miners under the age of 60 gainfully employed in one district (Bochum) of Germany's mining empire. Of these 81 (nearly 40%) work in the pits proper. He does not think that the ophthalmologist is justified in declaring a one-eyed miner unemployable. He should not, however, force miners who have lost an eye in an accident to return into the pits if they prefer to work above ground and accept the lessened income which goes with this type of work.

Taking 20/60 equivalent as the size of normal print and assuming that the visual acuity is 20/60 at 4 degrees from the fovea, one should at 16 in. have a reading "span" of 2.2 in. when fixating the center of a row of letters (Walton[174]). The problem, however, is more complex. Korte (1923), in his classic studies of the subject, found that so-called "masking" blurs out the inside letters of a group, while the most peripheral letters appear clear. He also found that words are better seen than nonsense syllables and that short words are seen better than long ones. Furthermore, since standard print does not consist of block letters, and since in most fonts letters are shorter horizontally than vertically, more letters are actually crowded into a line. Using 1/100 second of exposure, Walton (1955) found that approximately five words of five letters

can be read at a glance. The actual saccadic movement to carry the eyes from fixation to fixation takes about 1/60 of a second, while the reaction time necessary to initiate the movement is about 1/5 of a second. Taking 1/4 of a second as the duration of the average fixation, 1/50 second for the saccadic movement and 3/50 second for the return sweep to the beginning of next line, one can calculate why average college students read about 250 words per minute. Even if reaction time be 1/6 of a second, the number of fixations for a 10-word line reduced to two, and the return sweep, to 2/50 second, calculation reveals that no more than 1451 words can be read in a minute. Reading rates over this indicate that the reader is skimming.

Dr. Taylor,[175] the director of a Reading and Study Skills Center in New York, explains what he means under the terms span of perception, apprehension, and recognition, respectively, in reading. He has taken reading graphs of at least 10,000 persons. The tabulation of data of 5000 of these records shows decrease of fixations per 100 words from first grade to college and decrease of regressions in the same period, while the average span of recognition increases from 0.42 to 1.33 words. The average rate of comprehension is 340 words per minute at college level. Even college professors read no more than 500 words per minute, usually. Dr. Taylor gives the sound advice that "the important consideration in reading instruction is not speed but rather accuracy and precision so that comprehension may be adequate."

A book of reading difficulties "written for medical specialists" by Schubert,[176] an associate professor of education, seems to me one of questionable usefulness for them. After perusing it I find I know little new about the handling of this serious problem. Maybe "optometrists, psychologists, educators, parents, etc." will learn more from it, though I doubt that the first group will.

Since the opthalmologist is more and more often called in as a consultant in learning, especially reading, difficulties, it will well behoove him to know something about the behavior problems involved. A paper by Rapoport,[177] a psychiatrist, will serve as an excellent introduction. Learning difficulty, he states, is not a clinical entity in itself. "One cannot define a reading disability by saying it occurs in a patient with mixed dominance or that [it] really is an emotional block. This begs the question."

A study of the "relationship between field restriction and the speed of visual perception in reading" was made by Eames.[178] He considers "uninterrupted 30° central arcs" as normal. This "would permit more to be taken in at a given fixation," while a field restricted by, say 20 degrees, "would permit apprehension of a smaller amount due to the smaller extent of responding retina and its central connections." (Eames obviously forgets that only the very centrum of the visual field has the visual acuity permitting reading. Restriction of field does in fact reduce reading speed. However, the reason for this is the reduced ability to scan and to find the beginning of the next line when one line has been finished. This is the reason why restrictions of the visual field are "handicaps to learning.")

V. Clinically Useful Optical Techniques

Pearlman[179] describes a flat molded plastic plate with various-shaped holes, an eye template, which enables the ophthalmologist to outline the eye or its components and should prove useful to those who prefer labeled illustrations to extensive descriptions in clinical records. The instrument can also be used for the measurement of the pupils and of the interpupillary distance and for exophthalmometry. It is certainly a handy little device to carry in one's pocket.

Singer[180] built an electromechanical model of the human visual system in which lenses form the image of some object upon sets of photocells which represent the two retinas. From here, amplifiers carry impulses to electric bulbs which represent the brain, lighting them when stimulated. The

eyes are movable and are set in motion through a feedback mechanism which influences appropriate motors whenever there is an error in "fusion." Oscillations continue until the error is corrected. The authors believes that he will obtain by this analogy "insight into the recognition mechanism of neural systems" and "aid in brain damage localization"—hopes which probably no biologist will share. (It seems that, unless such "servo-mechanisms" are to serve as aids in teaching, the taxpayer's money on this type of "research" is utterly wasted.)

The use of monochromatic light in the ophthalmodiagnostic process has intrigued many. A short résumé of the history of these efforts is provided by Kornerup,[181] an author who has himself added considerably to the usefulness of this technique. In his last communication we learn of his adaptation of a monochromator to the new Zeiss slitlamp (constructed by Littmann) with which displacements of wavelength of as little as 0.22 mμ are recognizable. A photocell, applied to one of the oculars, makes it also possible to measure the amount of refracted light. (Discussion of the clinical usefulness of such an instrument is beyond the scope of this review.)

Luminescence by longwave ultraviolet (360-365 mμ) can be applied in ophthalmology, according to Stein,[182] to great advantage. He discusses several of the available instruments and many of the clinical problems for which its use is suggested.

When one sees the complex drawings of instruments, the graphs, and the formidable mathematical formulas in the paper by Buchmann-Olsen and Rosenfalck,[183] from the Laboratories of Biophysics and Neurophysiology of the University of Copenhagen, on the spectral energy calibration of a light-flash source used in physiologic optical experiments, one realizes (with some nostalgia for the past) how far we have gone since about 100 years ago the great Maxwell used a piece of white paper to reflect sunlight onto his spectrophotometer while making his epochal discoveries on color vision.

Though light sources of this type are unlikely to be used for medical photographic purposes, it might be interesting to know of a light source constructed by Fischer[184] which gives 40,000,000 candles per square centimeter with the half-duration of 0.25 milliseconds.

Askovitz[185] describes a versatile flashlight without batteries, adapted for connection with a transformer.

The same author[186] projects the image of the streak retinoscope upon the ceiling for use as fixation light in tonometry and tonography. The retinoscope is supported by means of a clamp to an ordinary laboratory stand, and the position of the light can be displaced at will.

The same author[187] made a quantitative ophthalmotrope from a government surplus navigating compass which makes it possible to rotate either "eye" independently about a horizontal vertical or sagittal axis and to read the rotations to the nearest degree.

A fixator for the version test (consisting of a handle, a 15 in. long arm attached to it by a rotary joint, and a white ball) was described by Fink and Fink.[188] The patient holds the handle, and his gaze is to follow the white ball as the arm is moved. This leaves both of the examiner's hands free in doing the cover test.

Unger[189] describes a new method of measuring the interpupillary distance (P. D.). He inserts discs with centrally placed tubules into the trial frame in front of the finally selected lenses and lets the patient manipulate the appropriate screws of the trial frame until he (the patient) sees the distance Snellen chart with each eye. If the lenses are too close together or too far apart, the patient sees the chart through two holes; these fuse into one when the discs are separated by the correct P. D. The test is repeated with a near reading chart to determine the correct separation of the reading glasses or near additions.

Wood[190] had the American Medical Association vision chart reduced to be read at 24 in. This is fastened to a transparent plastic sleeve which can be illuminated by

an ophthalmoscope (the head of which has been removed). Since the chart is reduced to one-tenth size, recording should be made in terms of 2/2 for standard vision. The chart offers a fairly accurate means of determining visual acuity at the bedside.

Berens and Taylor [191] find plastic spherelenses in clip-on frames useful in a great many instances. They use them for trial in accommodative esotropia and to relieve the temporary blur after cycloplegia. (These lenses are a companion set to the set of light plastic prisms, described by Berens in 1954, which many of us have found very handy.)

An ingenious instrument by Asher,[192] called a fixator, makes it possible to compare the two uniocular images in a natural manner, without making the patient look into a stereoscope or other contraption. He expects that his instrument "may supply a more accurate indication of binocular function than is afforded by the cover test or stereoscope." It also makes it possible to detect errors of fixation and unequal accommodation. (Asher calls this condition rare, while Siebeck [226] asserts that it is the rule in anisometropia. Maybe the instrument will contribute to the clarification of this issue.)

A new accommodation card and rule by Berens and Fonda [193] serves many purposes. Visual acuity can be tested with it for distance and near; pinhole vision can be checked; the near point of accommodation and convergence can be determined; the interpupillary distance can be measured, and the pupillary diameter can be ascertained. It also serves as a rapid visual field test for the detection of hemianopia or quadrant anopia and paracentral scotomas. It can be used too for mapping the blind spot and as a protractor. It has a string of 55 cm. length attached, on which 50, 33, and 25 cm. are marked by knots. This is useful for retinoscopy and some of the just-mentioned tests. All in all, a lot can be accomplished with just one little plastic card.

Two simple instruments, a fit-over cell to hold one or two additional lenses in front of each eye and an improved accommodometer, were presented by Costenbader.[194,195] The former instrument is to be used with the patient's own glasses and serves for addition of plus or minus lenses and prisms; the latter to be used to determine the near point of accommodation, visual acuity at 13 in., and the weakest correction essential for straight eyes and good vision in accommodatative esotropia. Only one symbol is exposed at one time (which is also seen by the examiner), and the symbols can be instantaneously changed.

The study of a paper by Magis [196] on the visual field is heartily recommended. This paper discusses the physiological basis of perimetry, the essence of the system of isopters into which one is used to subdivide it by the technique of quantitative perimetry, and the errors inherent in the instruments, the examiner, and the examined. An especially welcome feature is the easily understandable analysis of the theory behind the Goldmann perimeter (based on a modification of Ricco's law). The author calls the Traquair technique of perimetry "obsolete," and perhaps he is right. He finds it amazing that although Ferree and Rand published all their work (which laid the basis of quantitative perimetry) in the English language its impact was almost nil in the English-speaking countries.

A paper on the use of the Goldmann perimeter deals with one of its seemingly minor flaws. Misar [197] offers several methods by which it is possible to examine the perifoveal region which cannot be adequately studied with the original equipment. He claims that his method eliminates the not uncommonly registered discrepancies between visual acuity and visual field defects and permits the recording of differences in light perception from the periphery to the fixation point itself.

Meyer-Schwickerath (famous for the new technique of using light energy to coagulate

the iris or the chorioid and retina) and Bohnen [198] report an excellent new technique of campimetry. They present a projected grid and fixation target to both eyes while the examined eye sees a movable polarized test mark besides. The latter is (by proper polarization) made invisible for the fellow eye. "With the described method size and position of unilateral central scotomas can be estimated exactly."

Carbajal [199] suggests using a wand with a large oval test object, 50 by 70 mm., for plotting the blind spot. The obverse side carries a white O-shaped center disc surrounded by a white rim; the reverse side carries four white dots corresponding to the long and short diameters of the oval. The targets must be completely "submerged" if fixation is accurate. Four movements, right, left, up, and down will outline the blind spot quickly and accurately.

Zugsmith [200] describes a modification of the Harrington-Flocks multiple pattern field screener into a magnetic tangent screen, thus offering what a salesman would describe as two instruments at the price of one and the "known advantages possessed by fluorescent test objects."

François and Verriest,[201] who in a previous paper (1956) described the advantages and significance of scotopic campimetry, describe a new instrument for the study of the visual field in darkness. The stimulus is offered by a torch, the luminance of which can be regulated by two rotating polaroid filters and by a battery of photometric glass filters. The range of luminance extends from 10 to 0.000032 asb. A red fixation point is offered, and the field is charted either on a Bjerrum screen or on a plastic half-sphere, the perimeter of Astrodon.

Jayle and his group [202-205] discuss in several papers the advantages of mesopic scotometry. They use their own campimeter with adjustable luminances and find that the study of the central visual field under dim illumination reveals defects which are not apparent under photopic conditions. In scotopic campimetry they find the physiologic central scotoma a disturbing influence. They have also constructed an adaptocampimeter (a hemisphere of 50 cm. radius) with which analysis of dark adaptation, perimetric studies, and determinations of CFF are possible. (The discussion of the findings of these authors in several of their cases is not subject of this review. I might only mention that they found that, in the case of cataract, mesopic campimetry gives the best information about retinal function.) They find with their method a second break in the dark-adaptation curve at about 14 minutes from the beginning of the test.

The stereocampimeter of Haitz (who was the original inventor of this valuable method of clinical investigation) was much improved by Gärtner.[206] He made a stereoscope in which the patient's eye can be observed and his fixation checked. He printed the campimeter pattern on the back surface of the card, making it visible only to the investigator, and he uses fork-shaped objects so that while the patient sees one object the investigator sees another in the pattern visible to him. (The author introduced one unnecessary complication: He made the distance between the +5.00 D. lenses of his campimeter variable to make it conform with the patient's interpupillary distance, though it will be clear to all students of optics that the interpupillary distance in no way influences the working of a stereoscope, provided that the distance between the lens centers and the fixation points, respectively, is identical.)

Last year I reported about some Japanese trials adapting the ophthalmoscope, in a combination with a commercially available camera, for ocular fundus photography. Another such experiment is described by Liesenfeld,[207] who combined an ophthalmoscope with a Minox camera and a mirror-reflex angle-finder.

Fundus photography with electronic flash technique is described by Drews [208-210] in three consecutive papers. He adopted elec-

tronic flash to both the Nordenson fundus camera and an anterior segment photography unit. Since exposure time is 1/3000 second, the eye's own incessant fluctuations cannot blur the picture. Chromatic aberration is eliminated by the use of monochromatic light. In this manner, of course, only black-and-white pictures can be taken.

Zekman [211] describes a new hypostereo attachment ("hypo" because the lenses are set at less than normal interocular separation) for the Exakta V or VX camera for taking photographs at from 9 to 3 in. distance. Focusing is not possible, and for varying working distances supplementary achromatic lenses need to be added. Regular 35 mm. color or black-and-white film may be used.

Graham and Naylor [212] developed a method for the photographic measurement of the angle of squint. Photographs are taken with a fixed-focus camera. Three exposures are first made of the squinting eye with a fixation light placed centrally; three other exposures, with the fixation light moved some known angle laterally, and another three, with the nonsquinting eye fixating. Then the mean distances of the image of the fixation light from the limbus are determined. Calculations follow. This is an interesting piece of work, but it certainly has little practical value.

Prince [213] developed a new slit-lamp color camera with a special illumination system. He uses a xenon gas lamp which for focusing feeds on 15 volts, 10 amperes. For a controlled period of 1/12 to 1/120 second 3000 amperes can be "punched through" the lamp, producing an intensive flash. A real image of the lamp's arc is produced in the plane of the slit. The camera is mounted on the microscope head, and its lens has a maximum aperture of f 1.5.

An amazing new discovery by a research team of Polaroid Corporation is worth mentioning in this connection. Baxter, de Young, St. George, and Shurcliff [214] found a servo mechanism which *automatically* focuses and keeps in focus a high-power microscope with greater accuracy than is achieved visually. The method lends itself readily "to fully automatic operation, including 'tracking' a moving slide." The principle proper need not be discussed in this place.

Allen [215,216] published a new picture chart to test the visual acuity of small children. Details correspond to those of the 30 ft. letter E. He found that the characters were recognized by normal 7-year-old children at 20 ft. and by 3-year-old children at 15 ft. Some even did better. Each character is printed on an individual page of plastic material. All are held together by a ring binder. Amblyopia ex anopsia was called by Gundersen (1955) a preventable form of blindness. The author feels that every effort toward the earliest possible detection and cure is justified.

Allen [217] also suggested the use of a lorgnette-type occluder for testing children. ("Look through the hole in the fence" is a less forbidding request than "Cover one eye.")

Craig [218] had the good idea of pasting a +12.00 D. lens (with a −6.00 base curve) with Scotch Tape over the aphakic patient's own glasses. This serves as an inexpensive temporary lens shortly after surgery and gives useful, even if not always sharp, vision.

Hubbard and Hubbard [219] had the original idea of combining two of the well-known Edroy Magnifocusers in such a manner as to have about ×1.75 magnification below and ×3.5 magnification above—a kind of magnifying bifocal.

"Anaglyphic" glasses were found to be of definite usefulness by Berens, Brackett, and Taylor.[220] These authors describe "an entertaining and agreeable method of performing an otherwise monotonous type of eye exercise . . . by the use of the Duochrome Television Eye Exerciser." An illustration shows a patient "enjoying favorite TV program while performing diverging and converging exercises, using the plastic red and green Duochrome Cover

with aperture, red-green spectacles, and vertical and horizontal prism bars."

An optician, Suchsland,[221] gives detailed information about custom-made eyeglasses. He also produces custom-made occluders which really exclude all lights.

VI. Accommodation, Convergence, Oculorotations, Fixation and Its Anomalies, Amblyopia

Evidence has been accumulating lately that the refracting power of the eye increases by a measurable amount whenever it has no chance to focus at any sharply outlined distinct detail. One refers to this phenomenon as night myopia (since it supposedly occurs in complete darkness) or space myopia (since it also is said to occur in pilots looking into contourless void). The inference that accommodation takes place whenever there is no contour present to stimulate accommodation is not, however, easily acceptable and it is rather thinkable that the condition of accommodative "rest" is not identical with the condition to which one so readily refers to as "zero" accommodation. In analogy to Maddox' concept of tonic convergence, Heath (1956) introduced the concept of tonic accommodation, which, by necessity, has some value different from zero and which, in fact, might be inhibited when the eye, looking at a distant object, assumes the accommodation level usually called zero and necessary for sharp distant vision. The question has now been reviewed by Morgan,[222] one of our greatest authorities on problems of the accommodative mechanisms. After reviewing all the pros and cons of the question with his customary sharpness of analysis and elegance of presentation, this author tends to believe that "the normal resting state of accommodation is just equivalent to about 0.75 D. of clinical myopia" and that there exists what one might well call negative accommodation independent of the activity of the oculomotor nerve.

To study the accommodation status of the eye in a dark or empty surround is obviously not simple. Whichever technique (visual acuity chart, optometer, retinoscopy) is used to ascertain the status of accommodation, light has to be thrown into the eye and its effect might influence the status of accommodation. Westheimer devised an ingenious method to overcome this difficulty by using light flashes of 0.05 second duration. These flashes acted upon the subject's eye before his accommodation had a chance to change, while the apparent configuration of what he saw indicated whether his eye was underaccommodated, overaccommodated, or correctly accommodated at the moment of the flash. Westheimer[223] found accommodation against an empty visual field fluctuating around a mean value of 1D. The fluctuations themselves were also of the order of 1D.

Ophthalmologists interested in the history of investigation in general, or in the problem of the accommodative reflex in particular, should find unusual pleasure in reading a review of the literature of the last 100 years (with glimpses even into the further past) on the role of the sympathetic nerve in accommodation by Bonnet and Rougier.[224] It is excellent. There are ample quotations from the more important publications; Cogan's paper (1937), which for most of us clinched the argument in favor of dual innervation, is accorded its due prominence, and the studies of Olmsted and his school on the one hand and of Siebeck on the other, both of which gave what to me appears to be the final proof in favor of a sympathetic innervational factor, are well presented; so are practically all other important old and new contributions, which space does not allow me to mention. One finds it once more amazing that the great A. von Graefe already saw and in several papers (1855-1861) clearly postulated that the "tensor of the chorioid, like the iris, must have double innervation, oculomotor on the one side, sympathetic on the other." This review should be translated into English.

When fixation distance is marked on the x-axis of a Cartesian coordinate system in

meters and the necessary accommodation on the y-axis is given in diopters, one gets a rectangular hyperbola which approaches the axes asymptotically. The slope to this curve at any point indicates the *rapidity* of the necessary change of accommodation at the given fixation distance. It is, obviously, flatter at long fixation distances, steeper at short fixation distances. If the convergence necessary to bifixate any given fixation point is expressed in prism diopters rather than angles and if one again marks the fixation distances on the x-axis and the convergence angles on the y-axis, one arrives at a hyperbola with a shape identical to the previous one. Thus, according to Hill,[225] "When convergence is expressed in prism diopters . . . mathematical analysis of accommodation and convergence relative to their parametric variable, fixation or focal distance, becomes possible." (Hill correctly notes that the *actual* angle of convergence is not identical in symmetrical and asymmetrical convergence upon a given frontal plane. In fact, the angle keeps constantly changing with changing asymmetry of convergence as one tries to bifixate different points along the same frontal plane. He feels that this complication is "eliminated" when the prism diopter rather than the usual angular designation of convergence is used. Obviously the complication—if that it may be—is only masked in this manner, not eliminated, as the *actual* convergences are still not identical. The locus of all points bifixated under a constant angle of convergence is, however, well known. It coincides with the Vieth-Müller horopter circle, not the so-called frontal plane. The latter has no physiologic significance. What, if any, significance this new manner of charting accommodation and convergence has is, therefore, at the moment, hard to say.)

A small 100-page monograph by Siebeck[226] on the role of accommodation in binocular vision can be highly recommended for its excellent introduction into problems of accommodation and convergence. The author studied accommodation objectively (with retinoscopy) in one eye while the other eye was made to accommodate at print held at different distances, and he feels confident that the "dogma" of equal accommodative change in the two eyes cannot be upheld. He found that in unilateral myopia the myopic eye accommodates less (allowing for partial equalization of refraction for near vision), that in unilateral blindness the accommodation of the blind eye is lagging (just as is its convergence), and that in strabismus accommodative coordination is also lacking. Especially poor is the negative or distance component of accommodation and also the focusing for very close objects in a squinting eye.

Ogle and Martens[227] measured the change of convergence with accommodation (this is determined in the fusion-free position, with a fixed fixation distance and by the interposition of plus or minus lenses between eye and target). The slope of the curve which shows these measurements is the so-called accommodative convergence to accommodation (AC/A) ratio. They also determined the changes in convergence which (again in the fusion-free position) are not accounted for by the changing accommodative stimulus (these are calculated from data obtained by changing the actual distance of the fixation target). These additional changes are ascribed to the "awareness" of nearness, and the slope of the curve which expresses these values is called proximal converge to accommodation (PC/A) ratio. The authors used both the usual phoria (Maddox rod and prism) technique and a new fixation-disparity technique in obtaining their data. The AC/A ratio was found to be 3.5△/D. with both methods. The PC/A ratio 0.9△/D. with the first method and 1.5△/D. by the second. As a group, myopes showed greater AC/A ratio; the innervation necessary to cause a given change of accommodation seems to be greater in the myope. Convergence excess was associated with increased AC/A ratio, not greater PC/A ratio. In convergence insufficiency both were decreased. Two in-

teresting case histories (one wishes there had been more) indicate the bearing of these seemingly abstruse measurements upon everyday clinical practice. (Since the measurement of these ratios is sometimes important for the intelligent evaluation of difficult cases, one hopes that the authors will develop a simple standardized clinical method for their determination in an average office.)

Morris,[228] who seemingly has put an amazing amount of effort and enthusiasm into the study of the AC/A ratio, believes it to be a constant characteristic of the individual visual apparatus. He does not believe in the use of plus or minus lenses to induce accommodation but sets his reading targets at infinity (6 meters) and at seven inbetween distances to produce actual changes of accommodation. At each of the eight settings he makes five tests (not only the phoria test, as others do, but also the plus and minus lens blur test and the prism base-in and base-out blur, break, and recovery test), thus getting a profile of all these functions. He correctly states that one has to be clear whether the "A" of the AC/A ratio means actual accommodation (as in his test) or stimulus to accommodation irrespective of actual accommodation (as in the tests done with lenses) or, as a matter of fact, accommodative effort (which, according to Hill, the chief advocate of this concept, may be different from either). In any event, one is happy to know that the author with all his efforts was able to "provide optometric relief" (one wonders about the meaning of the adjective) in a number of cases.

In the symposium "Accommodative Esotropia,"[229] of the American Academy of Ophthalmology and Otolaryngology, the question of an AC/A ratio came to the fore repeatedly. Breinin doubts the existence of a consistent AC/A ratio. He thinks that "it is debatable whether such consistency occurs. . . . Although there is a convergence-accommodation relationship, there is not necessarily a ratio." Costenbader classifies accommodative esotropia into one group with "normal A/C relationship" and another with "abnormal A/C relationship." As a matter of fact, he seems to use this difference as the very criterion on which to start different courses of treatment. (He suggests Floropryl treatment only in the latter group.) And as to the result of therapeutic efforts, he states the first criterion of a good prognosis for cure to be "if the A/C relationship is good."

For whatever it is worth, this information should be not withheld from baseball enthusiasts: Davis and Jobe[230] found that good batters had a low AC/A ratio and good pitchers, a high one. Here you have, then, an excellent means of selecting the best players for either job with better than 80% efficiency! Typists with a high ratio have a "2 to 1 advantage" over workers with low ratio, while in electronic assemblers our authors found the reverse trend. In camera assembly work the eye with the medium AC/A ratio did best. (By the way, workers in the field are generally agreed that the ratio is not variable with age, while our authors report the interesting finding that around the age of 6 and again at around 47 there are humps in the otherwise linear and horizontal AC/A age curve.)

While, as one can see, there has been sufficient amount of interest in the effects of accommodation on convergence, less study has been devoted to the reciprocal relationship to what one might call the CA/C ratio. (See, however, my review[300] of the important paper by Heath.) Schapero and Nadell[231] found statistically significant increases in accommodation response on convergence stimulation in young persons, none in absolute presbyopes. (Of course, the absence of measurable accommodation in a presbyope does not mean that convergence could not have had an effect on the neuromuscular mechanism which in young persons induces accommodation. It only means that with the usual clinical tests no accommodation was found.) Proximal converg-

ence was also found gradually to diminish with presbyopia.

Passmore and MacLean [232] had an unusual opportunity to study the occurrence and management of convergence insufficiency in young adults (at the Walter Reed Army Hospital). To anyone who needs an elementary introduction into the techniques of measurement and treatment of this condition, the paper can be safely recommended. The authors statement that "a condition of absolute convergence insufficiency may be said to exist when the near point is greater [sic] than 9.5 cm. from the apex of the cornea or when there is difficulty in attaining 30 degrees of convergence" (the two values mean more or less the same amount of convergence) is somewhat dogmatic. Good photographs show the technique of several tests and exercises. The authors found Miss Capobianco's test of measuring the near point of convergence with a red glass in front of one eye rather useful. They are in favor of orthoptic exercises and find prismatic correction or surgery rarely necessary and inadvisable.

From a paper by Zettel [233] (which I do not wish to discuss) on his results on visual training (he gives, for example, base-out training, "in this order, with rotoscope, stereo-orthopter, possibly the tachistoscope and the metronoscope"), I want to quote the following relevant sentence: "The impression which the use of the several instruments makes on the patient or his parents should not be underrated." We are glad to know. The "specific muscle calisthenic unit" about which Mark [234] reports (and which, I am sorry to report, is manufactured by Keystone View Company, a company which I have always considered more serious) serves, I have no doubt, the same purpose. That it does any other good, I do doubt.

Alpern [235] introduced and removed base-in and base-out prisms suddenly before one eye and measured the horizontal movements of the eyes in terms of their rotational potential. The eye affected by the prism turned in the expected direction; the other made a smaller but fast version movement (a saccadic movement) in the same direction, returning (more slowly) to its original direction of fixation. He found a disparity between ocular rotation and the magnitude of the stimulus, the former always being smaller than would be expected. The magnitude of disparity increased as the stimulus increased.

Alpern, Ellen, and Wolter (see this review for 1956) suggested that the slow ocular vergence movements may be mediated by autonomic innervation to the extraocular muscles. To prove or disprove this point, Brecher and Mitchell [236] separated the sympathetic innervation to eye muscles in the cat and could, on stimulation, register no movement of these muscles. Sympathetic stimulation also did not consistently increase or decrease the tension of extraocular muscles produced by somatic nerve stimulation. (In the discussion of this paper both Adler and Wolter emphasized that this is only part of the story. The parasympathetic system might still have, and is more likely to have, to do with the presumed autonomic innervation. Besides, conditions in the eye muscles of cat and man are not to be compared, since the former have no muscle spindles. "I will hazard the guess," Adler stated, "that Alpern and Ellen's hypothesis is probably correct." Breinin does not believe in separate mechanisms for vergences and versions. "Tonus," according to him, "is not a mechanism which I could ascribe to the autonomic system at present.")

Ever since Burian's now classic studies (1939, 1941) on the subject, it is generally known that peripheral fusion is a powerful influence in changing or maintaining the relative position of the eyes to each other. An investigation by Nauheim [237] (cautiously titled as preliminary) led to the unexpected conclusion that "paramacula targets represent a greater stimulus to fusion than do central targets and that retinal locus rather than area stimulated determines the effectiveness of peripheral fusion." I can

only agree with the author that "further studies . . . are indicated" before this conclusion can be accepted. (Only in case the author meant "greater stimulus for fusion *movements*," would one, somewhat reluctantly, agree. Macular targets, when bifixated, offer no stimulus to *overt* fusion *movements*, since fusion has already been accomplished. Furthermore, the beautiful studies of Roelofs and Zeeman—reported elsewhere in this review—prove once more that not area but contour is the essential stimulus magnitude influencing (the visual process.)

Jampolsky, Flom, and Freid [238] studied the relation between fixation disparity and heterophoria under experimental conditions which approximated the normal visual situation. They found that the relationship is not a simple one and is not the same in esophoria and in exophoria. Disparity for distance fixation rose steeply with esophoria, while in exophoria its amount was largely independent of the degree of the deviation. In near fixation increasing fixation disparity was associated with increase of both exophoria and esophoria. The authors feel that the differing behavior of fixation disparity in exophoria and esophoria parallels the difference in focal suppression in the two conditions, inasmuch as there is a relatively fixed amount of focal suppression found in exophoria while its amount varies in esophoria.

A good review of papers on fixation disparity was published by Carter.[239]

The limits on uniocular movement were measured by Yamashiro [240] on 100 Japanese subjects. He used Wessely's keratometer to observe the eyes and Stevens' hypothesis (that the distance from the nasal to the temporal limbus is identical to the distance from either point to the center of curvature, giving an equilateral triangle) as the basis of his calculations. The average maxima were abduction 58 degrees, adduction 53 degrees, depression 50 degrees, and elevation 42 degrees. The maxima have a tendency to decrease with age. He found no difference between the sexes. Ocular dominance made no difference.

With all the efforts put for a century or more into the analysis of ocular motility, one would think that such a simple matter as the extent of the binocular field of gaze had long been established. Reading an interesting paper by Giroud,[241] one will be astounded that this is not the case. In fact, the only available data are the scanty ones given by Hering (1864) about his own eyes and somewhat more elaborate ones published by Schueller in 1875. The discrepancy between these two sets of data is enormous (Hering must have had very poor vertical motors), and Giroud, after elaborate tests, concluded that it is actually impossible to determine the *real* binocular field of gaze (the field *every* point of which can be fixated binocularly) with any degree of reliability. She resigned herself to determine the "practical" binocular field of gaze, the field which can be covered by fixation with both eyes open. She built an elaborate instrument, a perimeter with a radius of 1 meter, and used every possible precaution to have her data accurate.

Boeder [242] once more analyzed the general type of uniocular oculorotations, making it his purpose to elucidate their mechanics without elaborate mathematical machinery. For this he made a stereographic projection of the ocular equator and of the ocular meridians from the occipital point upon a plane tangent to the anterior pole of the eye and parallel to Listing's (frontoparallel) plane. On this map, the equator and any circle which does not pass through the occipital point (including all objectively vertical great circles), appear as circles, while all great circles (meridians) and all small circles which cross the occipital point appear as lines. He also made a model with a cross attached to the line connecting the posterior and anterior poles of the eye. The cross is erect when the eye is in its primary position. It stays erect in relation to the map whenever the eye changes fixation along any circle

through the occipital point, satisfying Listing's and Donders' laws. "False torsion is the angle that the vertical arm of the cross makes with the circles that represent the objective verticals in the map."

Westheimer[243] discusses eye positions and eye movements in mathematical terms which are beyond the reach of most of us. "An eye movement may be regarded as a rotation of the eye about an axis through the center of rotation." The scope of the paper covers the ground of the time-honored problems of ocular kinematics. The author develops equations for a single rotation which is equivalent to two finite rotations (which is the problem covered by Listing's law), and he also develops equations for the angles between primary horizontal ocular meridian and plane of regard and between the primary ocular vertical meridian and the true vertical plane through the line of fixation (which is the problem covered in the long controversy elicited by Márquez' contributions). This paper is called "Kinematics of the Eye." The time rate of change of eye position as a function of applied forces will be the subject of a paper called "Kinetics of the Eye," a problem which, as the author assures us, promises to be even more complex.

By asking their subjects to synchronize their eye movements with the rhythmic alternation of a pair of light spots or to follow these rhythmic changes, Polidora, Ratoosh, and Westheimer[244] found that the oculomotor system is poor in maintaining a rhythm and conclude that "eye position cannot be used as the input for a tracking system in any simple manner."

Professor Comberg developed a system to test the general visual efficiency of drivers, pilots, and others, examining (*a*) their visual acuity at different distances, (*b*) their color vision on a lantern instrument, and (*c*) their speed of recognition of details strategically placed at specified positions of the field of gaze. The latter measurement was used by Hager[245] on 300 healthy patients between the ages of 15 and 80 years to see how the "efficiency of gaze" changes with age. The data were analyzed with all the refinements of modern biological statistics, including, among others, the determined means and amplitude, the mean deviations from means, and the nowadays so popular *t*-test. The results show that the "efficiency of gaze" diminishes with age. A task which took 6½ seconds for those of age 15-45 required 11½ seconds at the age of 80.

Blodi and Van Allen,[246] in electromyographic studies, found active contraction of the external rectus muscle at the breakpoint of convergence associated with relaxation of the internal rectus muscle. This they too find to be a proof for an active divergence mechanism. They do not believe that a stretch reflex (as assumed by Breinin) could play a role in this phenomenon. The breakpoint of divergence did not produce any change in the electric activity of the tested muscles (the authors add cautiously, ". . . under the conditions of our experiments . . ."). They think that the small divergence amplitudes do not carry the eye beyond the range in which a change in electric activity could be measured with their experimental set-up. They found no change of electric potentials when during asymmetric convergence the tested eye did not move.

(Space will not permit me to report the discussion, which was at least as interesting as the paper itself is important. Some highlights are as follows: Breinin: "Divergence is an active process." Burian: "The tonus of the extraocular muscles is always in balance, even in comitant strabismus, except for frank paralysis." The record of increased activity of the lateral rectus muscle at breakpoint "does not," according to him, "necessarily imply the existence of a 'divergence center'. . . . Nor does it necessarily imply that the tonus of the extraocular muscles is regulated through proprioceptive mechanisms." Adler: "We are dealing not only with a relaxation of

convergence but with an active increase in tonus to both lateral rectus muscles.")

A series of two papers by Breinin [247,248] offers several examples of the usefulness of electromyography as "a tool in ocular and neurologic diagnosis." One can, by this method, better and far more objectively diagnose the transient improvement of myasthenia gravis by Tensilon. In palsies of extraocular muscles one can establish the site and character of the lesion. Electromyography suggests, e. g., that the so-called progressive nuclear ophthalmoplegia is more closely related to muscle pathology than to neurologic involvement.

Since Cooper, Daniel, and Whitteridge have finally established the presence of muscle spindles in the extraocular muscles, the problem of ocular muscular proprioception has become once more acute. Breinin,[249] by electromyographic studies, has found that the extraocular muscles have, in fact, a tension-recording apparatus which is significant for their adjustment and for the position of the eye. He makes it clear that this "proprioception" does not necessarily include "awareness of position" and that the term proprioception in the wider uses must include all kinds of feedback mechanisms which control muscle discharge. Only in this sense will his experiments offer a proof for the existence of proprioception in extraocular muscles.

To his recording instrument, Breinin [250] has now added a wave integrator which measures the total energy output of the muscles in a given time interval. With his new technique he has already made some significant observations, several of which will be briefly mentioned. He found "there is no inner rational basis for the belief that the vertical recti [Lancaster insisted in calling them rectus muscles] are active accessory adductors or the obliques active accessory abductors in horizontal rotations of the eye." Such accessory action "can occur only in consequence of the relation of [the] muscle plane [of an individual vertical motor] to the center of rotation of the globe and is not due to a purposeful increase of innervation." During convergence below the horizontal plane the inferior rectus is actively firing. When accommodation is induced in one eye by interposition of minus lenses, the internal rectus of the (covered) other eye shows increased levels of firing. The characteristic fall-out of innervation and the response to Tensilon in myasthenia gravis are readily measured.

In another communication, Breinin [251] reports on his studies of the ocular electromyogram during anesthesia and sleep. In general anesthesia all muscular activity ceases when a sufficiently deep plane was reached. As the level of anesthesia lightened, individual motor units started firing. In local anesthesia there was a progressive disappearance of motor units with decreases in amplitude until finally the muscle became electrically silent. During sleep he found intermittent irregular runs of units with brief intervals of electric silence.

Electromyography has further been used by the same author to analyze the interplay of accommodative vergence and fusional vergence in experiments with the haploscope or with plus or minus lenses used to change the accommodative stimulus. Breinin [252] concludes that all adjustments are made centrally while the final peripheral common path acts in terms of a "clear-cut reciprocity mechanism." No cocontractions occur. In the long controversy over the divergence mechanism, Breinin is on the side of those who consider it an active process.

Electromyography has found its way into Japan: Kamouchi [253] reports on electromyograms of palsied extraocular and levator palpebrae muscles in 56 cases. He reports abnormal discharges, reduction in number of spike discharges, and low-amplitude neuromuscular unit voltages. Fibrillation voltage (a useful diagnostic finding in denervation of other skeletal muscles) could not be ascertained. Reinnervation voltage, which appears generally in the course of

regeneration of peripheral nerve tracts, showed itself readily on paretic eye muscles. Grouping voltage (which, in the skeletal muscle, is explained as due to decrease of proprioceptive impulses) could be found in a few cases. In cases of a nerve palsy of high degree uneven recruitment was often recognized.

Another example of the usefulness of this interesting technique is offered by a publication of Lincoff, Breinin, and de-Voe.[254] Hofman and Lembeck (1952) found that succinylcholine injections cause contraction of the extraocular muscles, and Lincoff and associates (1955) proved that by so doing they increase the intraocular pressure. (This obviously meant that the use of this interesting drug is dangerous in intraocular surgery.) This newest publication proves on nerve-muscle preparations of the inferior oblique muscle and the gastrocnemius in dogs and cats that the injection of succinylcholine in fact causes a sustained contracture of the former muscle while the latter enters into a flaccid paralysis. Electromyographic studies of the lateral rectus muscle in cats confirmed this paradoxical response of an extraocular muscle. The authors also had occasion to do electromyographic studies of humans and found that the contracture occurs only in the unanesthetized or lightly anesthetized patient. In deep anesthesia, succinylcholine seemed to have no effect upon the extraocular muscles.

Anyone interested in nontechnical details and in need of an introduction into the subject of electromyography in general will, by the way, find this in a paper by Post,[255] from the department of electromyography at St. John's Episcopal Hospital in Brooklyn.

An extremely interesting paper by Enoch[256] presents a new theory for the genesis of amblyopia. To be sure, the theory is based on the study of a single case (a highly trained observer, it is true) with high myopic astigmatism. The author studied the so-called Stiles-Crawford effect in both eyes of this observer. While the profile of the effect was found normal in the good eye (with 20/20 vision), that in the poorer eye (with 20/40 vision) was definitely distorted. The generally accepted explanation of that is that luminous efficiency depends on retinal orientation. The amblyopia in this case might then have been caused by congenital disorientation of the sensory elements in the macula. Should this be true even in some cases of so-called amblyopia ex anopsia, then both the theory which is to explain its development (nonuse) and the orthoptic approach to its treatment would be open for reappraisal.

Enoch's subject, Grosvenor,[257] based an interesting candidate's thesis for a Ph.D. degree upon his own studies on his amblyopic eye. He reports especially on brightness discrimination data obtained within a wide range of background luminances and exposure durations. Except at the absolute threshold level, he found the discrimination ability of his amblyopic eye decreased. This was true for both the light threshold and the recognition of the form of the presented stimulus.

Fixation patterns vary, according to Hauser and Burian,[258] in strabismic amblyopia. Studying the fixation of the amblyopic eye with several modifications of the so-called after-image transfer test of Givner and Brock, they found that if normal retinal correspondence is present, some patients will foveally fixate with either eye. Other patients, also with normal retinal correspondence, behave much in the manner described by Givner and Brock when the fixation stimulus to the amblyopic eye was of low intensity. They corrected their fixation error under the influence of a stronger stimulus. In two cases, also with normal retinal correspondence, there was a peculiar displacement of the "transferred" afterimage, whichever eye fixated. One patient with normal correspondence was not able to perceive the afterimage when he fixated with the unexposed eye. Patients with abnormal correspondence "trans-

ferred" their foveally acquired afterimage in their usual correct (or corrected) way.

Givner and Brock [259] do not agree with this exposition and find fault with several of the conclusions. (To me, the actual issue of the controversy is not quite clear. Hauser and Burian agree that in amblyopia there is a weakness of fixation and that this weakness might be a relative one only. A priori one will expect that alternating squinters will be less likely to experience the afterimage impression upon one eye when the other eye takes over fixation. However, this point can only be decided in sufficiently extensive clinical tests.)

A paper by Böhme [260] clarifies further details on the nature of eccentric fixation. There is, for instance, the case of an amblyopic squinting eye which in the primary position saw 5/20; in abduction, 5/35, and in adduction, 5/7. The visuoscope revealed that, in abduction, fixation was carried out with a retinal area near the disc; in adduction, with one near the macula, and in the primary position, with an area between the two. Böhme feels that eccentric fixation has a motor component and is not exclusively a sensory phenomenon. He thinks that most strabismus is, to a degree, noncomitant and, as in the above-quoted case (which he considers to be a case of weakness of abduction), a paretic factor adds to the inability to fixate foveally. This prompts him to do early surgery to improve conditions for pleoptic therapy.

In connection with this publication a paper by Krause [261] is worth mentioning. This author, giving his results with the treatment of eccentric fixation according to Cüppers' technique, notes that the afterimage of the stimulus supposedly placed by the orthoptist around the fovea sometimes appears to the subject to be somewhat eccentric from a fixated mark or letter around which the afterimage is expected to center. (There are no accurate figures on the extent of this displacement given, since this seemed to the author to be only an incidental finding.)

In unilateral amblyopia Mackensen [262-264] found increased unsteadiness of fixation demonstrable by oculography and due to flicks without definite direction and nastagmoid vibrations. Study of the eyeground with the new directional ophthalmoscope does not always give the same picture and is therefore not fully reliable. While the ophthalmoscope only indicates the retinal area used for fixation, the details of ocular behavior during fixation are better revealed by oculography. Gaze movements are also disturbed. The unsteadiness of fixation indicates an increase in the extension of the area used for fixation, the macula having lost its physiologic position of preponderance. The inaccuracy of gaze movement is a sign that for the very same reason the eye cannot safely gauge the desirable span of oculorotation. Modern pleoptic treatment, this author finds, influences both fixation and gaze movements beneficially. The oculographic tracing offers a more objective method to demonstrate the improvement than simple registration of the final visual acuity.

When a squinter with so-called anomalous correspondence looks through a red glass with one eye and through a green glass with the other eye, upon an undifferentiated white surface, he sees part of the surface red, part of it green, corresponding to the direction of the respective foveas. This interesting fact is described by Swan and Wahlgren [265] and is called by them an "anaglyphic" phenomenon. (Actually, "anaglyphs" are the superposed stereograms which one looks at through an "anaglyphoscope"—usually Polaroid filters or red and green goggles. Thus, the phenomenon should perhaps be called "anaglyphoscopic." This phenomenon obviously proves that when there is no contour of attention to look at with one fovea there is nothing present in the stimulus configuration to suppress the impressions through the other fovea. It also shows that the behavior pattern called anomalous correspondence has nothing to do with some new

type of retinal correspondence or coupling or binding. This unfortunate term covers the fact of essentially *correct* egocentric localization of ambiocular impressions in spite of the faulty relative position of the two eyes.)

Monocular diplopia in strabismic patients results, according to Roelofs,[266] from an "abnormal binocular cortical binding with simultaneously an optical localization via the cortical representatives of the retinal elements of the eye which receives the stimuli and an optical localization due to the abnormal binding via the representatives of the retinal elements of the other eye." Monocular diplopia can in no way arise in a normal eye with normal binocular binding. This obviously correct statement has lately been contradicted, especially by Linschoten. Our author, in an elegant analysis of specially designed stereograms (based on Panum's limiting case and allegedly proving that monocular double localization is possible even in normals) disposes with this most unlikely explanation. If in these experiments with stereograms normal persons see two of certain details, then the reason is because to at least one eye two of such details have been offered.

Harada[267] reports the amazing fact that in Japan more cases with divergent squint (59%) have anomalous correspondence than cases with convergent squint (17%). In convergent squint, anomalous correspondence is rare in intermittent cases. The opposite is true for divergent squint. Divergent squint with anomalous correspondence started after the sixth year of life in 31%. Anomalous correspondence *and* amblyopia were found in 6% of squinters. Thus, the two conditions are not mutually exclusive. The peak frequency of anomalous correspondence occurs among divergent squinters with 20 to 24 degrees of deviation. Interesting are statements about panoramic vision in divergent squint. Harada found that one of his patients saw 6/24 with the deviated eye in line with its fovea while the other eye was fixating the 6/6 line straight ahead. In fact, he considers that a "congenital sensory anomaly, such as panoramic vision . . . constitutes the cause of squint." Together with dominant anomalousness of correspondence, normal correspondence would be demonstrated in 70% of these cases by the afterimage test, even before any therapy was introduced. "Restoration of normal correspondence by the treatment does not mean that retinal correspondence changes its type by adaptation."

Lang[268] believes that the anomalous sensory relationship between the two eyes will influence the final position of the eyes after strabismus surgery. He found that the eyes of patients with anomalous retinal correspondence will show a tendency to return to the preoperative position. This, he believes with Hamburger (1945) and Halldén (1952), is due to fusional movements which are present in spite of the anomalous sensory relationship.

It is not in my department to discuss the remarkable change in outlook of continental orthoptics at a time when in Anglo-American orthoptic literature a remarkable restraint became the order of the day. (P. Knapp: "We no longer treat anomalous correspondence orthoptically," *Survey Ophth.* 2:325, 1947). However, there is no strict borderline between the material to be reviewed in this and in next month's issues, and since many of the results touch upon problems of basic visual physiology, a certain amount of duplication is unavoidable.

First, a paper by Görtz[269] should be mentioned, just to emphasize the difference of the present European orthoptic climate. This author reports to have changed correspondence anomalies in 79.5% of his cases. He is very radical in reoperating in cases in which there is a small residual convergent angle of squint once sufficient fusional convergence power has been developed, since he is more afraid of the development of a secondary correspondence anomaly

than of postoperative divergence. His argument is convincing.

The most revolutionary of the new thoughts are the ones relating to the role of occlusion in unilateral amblyopia with eccentric fixation. According to the opinion of Böhme (1955) and of Bangerter (1953), occlusion of the fixating eye is absolutely contraindicated when the squinting eye manifests eccentric fixation. That the stressing of this absolute contraindication is unjustified has been proven by a beautiful experiment of nature reported by Mayweg[270] from Amsler's clinic in Zurich. A 35-year-old woman had had her good eye enucleated because of malignant melanoma, though the other eye had 1/60 vision with eccentric fixation. The author gave this patient fixation training with the Cüppers euthyscope, and she had central fixation with 0.4 to 0.5 vision for distance and 0.6 for near in seven days! (One wishes a control experiment were possible to find out what results there would have been without the euthyscope training.) This author is also in favor of occlusion in anomalous retinal correspondence, and, while Lang (see the foregoing reported paper) often found a return to the original position of squint after surgery, Mayweg found no such change or a change to the better if the occlusion of the eye operated on was carried out for several months.

Those interested in the subject will also find a short résumé of recent papers on the treatment of eccentric fixation in the column "Strabismus and Refraction" conducted by Schlossman.[271] The methods of both Bangerter and Cüppers are adequately covered.

This paramount problem of orthoptics, amblyopia ex anopsia, was attacked in an unusual manner by Kupfer,[272] who found seven adult male patients aged 18 to 22 years, with amblyopia in one eye, willing to have their good eye bandaged for four weeks. (The work was done at a U. S. Air Force Hospital, where these persons must have had a leisurely time.) When fixation of the amblyopic eye was eccentric, the patients were taught macular fixation in a manner reminiscent of the European method (which, however, the author seems to have developed independently) with the aid of the pantoscope and a pinhole glass. Repeated mappings of the blind spot and of areas of suppression gave definite indication if and when central fixation was finally achieved. In five of the seven patients visual acuity improved to 20/40, 20/30 (two patients), 20/25, and 20/20, respectively. (I think this is an unusually fine piece of work, and it shows that Bangerter and Cüppers, with their strict contraindication of bandaging the good eye, might not have found the only road to salvation.)

A paper by Mayweg[273] is interesting for several reasons. He had the unusual opportunity to see three adult patients who each lost their good eye and regained good vision in the amblyopic eye with euthyscope treatment. He did of course not occlude the amblyopic eye in the course of treatment. He achieved definite success in children with amblyopia, despite eccentric fixation, with euthyscope treatment *and* occlusion of the amblyopic eye during treatment. And he agrees with Cüppers and Haensel that normal binocular vision (with stereopsis!) can be achieved, even in cases of anomalous correspondence, in about two-thirds of the cases. His treatment seemed to have only failed when the strabismus started at birth. He hospitalized most of his patients for the time of treatment.

Even the most intensively reeducated case of amblyopia needs "post-cure" according to Sédan.[274] Improved visual acuity for single optotypes does not yet mean efficiency in reading, as separate letters are always better seen than sequences of them. Sédan published in book form and also discusses in a paper of real Gallic charm a number of exercises he designed as "post-cure." The most original method of his is proofreading with the reeducated eye and the solution of all kinds of picture puzzles. (It seems that with all his enthusiasm for "euthyscopie," Sédan still believes in bandaging the good

rather than the amblyopic eye. He, too, seems to believe in the importance of eye-hand coordination, and his book contains a number of "stitching" designs for its enhancement. On the other hand, he forbids the use of pointer or pencil during the proof-reading exercise—a point which is not quite clear to me.)

VII. Visual Perception, Stereopsis, More About the Luneburg Theory, Aniseikonia

The respective roles of past experience and innate organizing processes in visual perception were once more reappraised in the light of present-day knowledge by two psychologists, Zuckerman and Rock.[275] They conclude after a rather complete examination of the existing evidence that "segregation and shape of visual forms are given by innate organizing processes. Percepts may be modified and enriched by experiential factors but the effects of such factors presuppose the prior existence of usual forms . . . . Perceptual organization must occur before experience. . . . Despite changing motives and emotions, phenomenal color, form and space remain remarkably stable and generally correspond to the objective situation."

Diametrically opposed to this (in my view correct) appraisal, which in analyzing some 80 references covers almost all of the more important contributions to this great controversy, is a statement from a rather authoritative source, (the presidential address of Ruedemann[276] to the Section on Ophthalmology of the American Medical Association), in which we read: "The fact of the matter is that seeing is a learning process. No one is born knowing how to see. . . . No one learns to see instinctively. . . . When we measure vision we obtain the present visual intelligence level of that individual. . . ." Ruedemann's rather radical stand in this controversy naturally leads him to the (in itself correct) emphasis on neural factors in the development of squint. "Again I will state that muscle surgery is not the answer." The historically minded will read with interest a reference to "the charlatan Taylor [who] started us off on the wrong foot, or perhaps the wrong eye, by cutting eye muscles. . . . Since that time ophthalmologists . . . have thus been muscle inclined."

(They will, by the way, find an interesting short biographical note on that most intriguing charlatan and scientist (which he, to some degree also was), the "Knight Errant, John Taylor," in a paper by W. Münchow [*Klin. Monatsbl. Augenh.* 129: 404-410, 1956], and in Polyak's book they will find not only his picture (Fig. 77) but a description of his ideas on the mechanism of binocular single vision "which were remarkably modern." In fact, Figure 78 in Polyak's book, reprinted from Taylor's "Mechanismus," 1750, clearly shows the partial decussation of the optic nerves. "Whether original or borrowed, this view was subsequently developed by Johannes Müller, H. Wilbrand, and others into the modern 'theory of corresponding or syndynamical points'." Taylor did, seemingly, not start us off on an entirely "wrong foot.")

The age-old "problem" of erect vision with inverted retinal images was, among other fundamental problems, once more attacked, and in really Gallic fashion, by Professor Borissavliévitch,[277] *chargé de recherches au Centre National de la Recherche Scientifique.* One will agree with his contention that the first is no problem at all. The author states that the retinal images must be inverted *in order* that one see erect and proves this by inverting an object which now obviously has an "erect" retinal image, while, lo and behold, we see it inverted. The reason for all this is that the eye has to move *upward* to see, foveally, the upper detail of an object, and *downward* to see the lower details. *"We might thus conclude that a point is there where we turn our gaze."* (italics by the author). While one moves one's gaze upward, toward upper details of a vertical line, the retinal image of the formerly foveally fixated lower detail moves also upward across the retinal surface, while the upper moves downward.

"*Voilà*, why it is necessary that the image of this vertical line be inverse on the retina, so that we see it erect, running from below upward." (Similar considerations explain why an object is seen on the right side while its image actually is in the left half of the retinal image.) "The problem, non-existent as we have just shown, was posed because the physiologists, though recognizing that the eyes are in 'perpetual motion', studied the phenomena of vision as if the eye were *immobile* and the retinal image *static*" (italics by the author). This explains the grave errors they have committed in the interpretation of the visual angle and also of stereopsis. They (the physiologists) affirm that the cause of the latter is to be found in the retinal images being different, while they are not. The convergence and accommodation of the eyes upon every point of an object *prevents* the images from becoming different. Assuming that the eyes are immobile, and visual perception simultaneous rather than successive, the physiologists confounded or identified the visual apparatus with a stereoscope. One has to revise, our author concludes, the classic concept of "retinal image" and replace it by one resultant from facts of physiology, liberating it from the whole physical or mathematical concept. This will also explain, among other things, why we see lines straight, though their retinal images are curved.

A paper on stereopsis tests by Anapolle [278] does not purport to contain anything new but will be interesting to the novice as an introduction into the methods of producing stereoscopic effects and as a short inventory of the commercially available stereopsis testing devices. One of his conclusions may be quoted: "It is established in the field of visual science that stereopsis represents the height of development of binocularity in the evolution of man."

Efron's [279] experiments confirm the work of Langland (1929) according to which simultaneous retinal images are not the *sine qua non* of stereopsis, as with a sufficiently high rate of alternation of viewings by the left and right eye a sense of depth can still be realized. A scene flashed in *one* eye obviously sets up a "percept" which persists for a measurable period and can be utilized by the brain for stereoscopic fusion if a slightly different coordinate stimulus is presented to the second eye within a critical time interval. (I am sure that with the known persistence of vision everybody expected this to be the case. One might refer to the fact as an example of "temporal summation." It is, however, just an example of plain "fusion." And it is another proof that stereopsis is not based on "replacement.")

Ten Doesschatte and Kummer [280] measured the heterophoria of 5000 applicants for pilot licenses of the age 17 to 22 years and with 6/6 or better vision at the National Aeromedical Center of the Netherlands. More than 30% of them were orthophoric, and another 33% had an eso- or exophoria of not more than 1△. Depth discrimination was measured with a modified Helmholtz three-bar instrument at 6 meters distance. The overwhelming majority of this elite group had superior depth discrimination in this test, though many performed in a mediocre manner and about 1% of them failed it totally. On the other hand, there were candidates with esophoria or exophoria up to 14△ whose performance was excellent.

A rather unique study by Danielson [281] is offered as a "pilot paper . . . to indicate the many facets of the problem of the relationship of fields of vision to safety in driving. It would appear that defects in the driver's field of vision are a very minor cause of accidents. . . . If a physically and mentally sound driver obeys the traffic laws, intelligently takes precautions and has a visual acuity of 20/40 or better . . . he can operate an automobile with safety . . . if his total field is as low as 50 degrees."

Roelofs and Zeeman [282] studied the influence which objects seen binocularly (in a stereoscope) exercise on the apparent size

and distance of monocularly seen details. They found that both (the apparent size and apparent distance) "adapt" themselves to that of objects seen binocularly. They conclude that "difference in apparent size in retina images of equal size, and difference in apparent distance are due to a tension between the convergence impulses which tension is aroused by the concerned retina stimuli." They also found that retinal images of equal-size objects in a higher position or in a more temporal position are estimated to be larger and further away. "This is based on the fact that in the visual field, lower and more nasally situated objects more often give rise to a convergence impulse than higher and more temporally situated objects." They also found that "objects on the right are estimated to be larger and farther away than objects lying more to the left."

A paper by Bleything,[283] from the Gunther Branch School of Aviation Medicine, suffers from a deplorable confusion of the terms "stereopsis" and "distance localization," due to obviously only second-hand familiarity of the author with the works of the classic writers. Wheatstone (1838) has indeed laid the basis for our understanding of stereopsis (and, by the way, coined the word for it), while Wundt (1859-1861) and Hillebrand (1894) were interested in an entirely different problem, the role of accommodation or convergence (or both) in estimating the distance of objects (which, of course, has nothing to do with Wheatstone's work on, and his concept of, stereopsis). As a matter of fact, part of their work was carried out with monocular observation. Bleything's experiments aim at the same problem. (He tried to determine the apparent distance of the fused "image" of two patterns, each presented to one eye under the condition of crossed or uncrossed disparity and varying their separation.) They have nothing to do with stereopsis, and his term "stereoscopic size" is meaningless. His main conclusion is the following: "Stereoscopic size increases with stereoscopic localization distance and at a rate slightly faster than the rate obtained if the size is predicted from the visual angle subtended at each particular distance measured."

An interesting new method, walking about 50 yards toward a target placed 1000 yards away, was used by Bailey[284] to determine "visual projection." (The experimental concept is excellent; the terminology, deplorable. In fact, the author himself notes the absurdidity of the idea that an observer constructs an image which he projects somewhere into the space surrounding him. What the author obviously studied was sensory-motor orientation.) He found that in normal binocular persons "projection" proceeds parallel to the bisector of the angle of convergence; in one-eyed subjects, parallel to the line of sight of the main eye; in squinters with normal correspondence, parallel to the line of sight of the eye preferred for fixation, and in squinters with anomalous correspondence, parallel to the line of sight of the eye used.

A compilation of material on some visual problems of flight from the literature, especial the *Journal of Aviation Medicine*, the "Flight Surgeon's Manual" (AFM 160-5, 1954), the "Aircrew Effectiveness Reports of the Eighth Air Force" (1954-1956), and the publication "German Aviation Medicine in World War II," by the Department of the Air Force, was published by Arner,[285] U. S. A. F. (MSC) and is worth reading. One will find much interesting detail. "Due to the fairly rigid entrance requirements for pilot training, it is common belief that an airman must have superior visual capabilities. . . . To a large extent this is not true. . . .He must have reasonably good visual acuity and be free from any of the impedimenta to comfortable vision that are often encountered, but this is all that is required. . . . Stereopsis has been found to be considerably overrated. . . . This is not to say that a smooth landing does not require perception of depth. The point is that it is not the binocular parallax, the classical stereopsis, which is used, but the apprecia-

tion of motion parallax." In fact, Emerson (1955) found it to be the angular velocity of ground objects which gives the most important clue of distance estimation. The requirements for normal color vision have also become less rigid. Of greatest practical significance seems to be maintenance of good dark adaptation during flight and adequate oxygen pressure. There are further interesting details on explosive decompression and its effect upon vision, on the effects of positive (head-to-foot) and negative (foot-to-head) acceleration on vision, on vertigo, the autokinetic effect, vibration, flickering lights, windshield and cockpit engineering, the wearing of corrective glasses, the red-hyperopia caused by the prevailing red illumination in the cockpit, and the visual problems introduced by supersonic speed—all problems about which ophthalmologists need to be intelligently informed.

Although one likes to adhere to the dictum *de mortuis nil nisi bonum,* one might not quite agree to the publication of a paper of questionable value just as an act of piety. The late van Albada,[288] an "amateur stereophotographer" (and, by the way, inventor of an improved stereoscopic viewer) makes the mildly ridiculous suggestion that illuminated objects possibly "radiate certain undefined rays capable of causing a sensation of their distance." He prefers this explanation of the distance perception to experience, "since a one-eyed person can orientate himself quite readily in a totally foreign surrounding." The experiments which the author devised to support his views are far from being new, and their results have all been well explained without resorting to "stereotronic radiation" (whatever that term might mean).

In a paper reported in last year's issue of this review, Ogle and Groch questioned the validity of Verhoeff's observations regarding stereopsis under the condition of unequal liminosities of the images in the two eyes. The validity, on the other hand, of their conclusions was (as could be expected) questioned by Verhoeff,[287] and the issue is certainly open to further considerations. (As a matter of fact, one part of the important contribution of Gillott [295] to our knowledge of stereopsis and inequality of retinal images deals with this very question.)

There will be, at last, available to the German reader a concise and clear presentation of Luneburg's theory of binocular visual space and of the Ames experiments with distorted rooms which led to its formulation. It is an astounding feat to present this material in German, retaining the clarity of the English in which these concepts were first formulated. The feat was achieved by Boeder.[288] For all those who have had to work themselves through the nebulous complexity of the great works of Tschermak, it will be a pleasure to read Boeder's short piece.

Ames' distorted rooms have once more brought the problem of stimulus equivalence and the inherent uncertainties of the ordinary stimulus situation to the fore of scientific interest. Professor Oldfield,[289] of Oxford University, gives an interesting analysis of these uncertainties. Only by "supplementary sources of information which include estimates of probability derived from past experience" can one judge "the general geometric structure of the immediate scene from its dominant perspective features" or "the actual luminance of objects from their apparent brightness." An interesting observation is worth remembering: Oldfield finds that "in uniform illumination the range of brightnesses encountered is only as 1 is to 9. Anything outside this range tends to be perceived either as a self-luminous source or as a hole in the surface or one of differences of illumination in different parts of the field."

The impetus of Luneburg's contribution has, by the way, not lessened with the years. Blank,[290] one of Luneburg's early students and collaborators, modified and reconstructed his theory, expressing himself in terms which even the nonmathematician will understand and, if interested in this great advancement in the understanding of

space perception, read with pleasure. Shipley's [291,292] presentation is much harder to follow. He elaborates on one of the salient points of Luneburg's work, the interdependence of r, the sensed distance of a bifixated point, P, in visual space, with γ, the angle of convergence, or, as mathematicians would express it, on the $r(\gamma)$ function. Some of the important statements are as follows: "There is nothing in our visual space to correspond with the purely intellectual concept of infinity. All visual experience is finite . . . is bounded. . . . The origin of visual space cannot be placed anywhere at will. It is the self which sees . . . and must, perforce, contain the origin." Shipley, thus, rightly abrogates Hering's nuclear point from its unwarranted place of eminence. He recalculated all data so far collected on the distance and parallel alleys (see this review for 1956,[300] especially page 908), adding his own experiments, and, while he is convinced that "equidistance" alleys are outside "parallel" alleys, it seems to him that this still does not make visual space hyperbolic beyond all doubt. "Visual space is perhaps more likely of *positive* curvature. . . . The original Luneburg suggestion definitely requires modification."

Blank's modifications are more down to earth and of greater clinical interest. When looking from a point P_0 seen under an angle γ_0 of convergence one turns to another point P, seen under another angle γ of convergence, the number of retinal elements simulated by the transit is counted by some comparator mechanism registering the possible disparities. When there is no displacement disparity, γ_0 remains unchanged and both points P_0 and P appear to be at the same distance. Blank thus explains the $r(\gamma)$ function in terms of retinal physiology. The locus of "all points which are sensed as forming a circle centered at the observer," Blank calls the circumhoropter. In normal persons this coincides with the Viett-Müller horopter of constant convergence, while in aniseikonia the coincidence is nonexistent. Here the eye in which the retinal image is larger must obviously turn fewer degrees before the same number of retinal elements are scanned over in both eyes.

This r (γ) function (the dependence of sensed distance on convergence) is, of course, only a postulate of mathematicians; it will gain value only if convergence can, in fact, be proven to offer a sensory clue. (A sensory clue need not be one the effects of which arise into consciousness. This has repeatedly been emphasized by the psychologist Woodworth (1938) and, recently, also by Breinin.) Siebeck,[226] in his small monograph "Accommodation and Binocular Vision: The Synergism of the Functions of Depth Perception," deals with this important issue. (Other details of this excellent piece of work have already been discussed in another section of this review.)

As could be expected, (see this review for 1956,[300] p. 908), Squire's conclusions concerning the nature and geometry of visual space (especially his findings regarding the so-called distance alley), have not remained unchallenged. Shipley and Walker [293] raise the interesting point that even alley experiments carried out in the dark are in fact photopic. "Truly scotopic (i. e., rod vision) alleys cannot be measured at all because of the markedly reduced peripheral acuity and the increased tendency toward autokinesis." They also question the validity of conclusions in which the observer's attitude can shift the results one way or another. But, first of all, they question the relevance of data (the accuracy of which they do not question) obtained in an illuminated room upon Luneburg's theory of binocular visual space, since "such a configuration possessing rich monocular perspective clues [and] cannot be said to be exclusively, or even predominantly, binocular."

One will in a discussion of this type seldom expect that one of the discussers fully convinces the other of error; in fact, Squires [294] in his reply contests the validity of most of these statements. He finds "attitude" an integral part of every observation,

and since "man does not carry on a mole-like existence" he finds study of binocular vision under white light justified. "It may very well be that in searching for the Riemannian metric of binocular space we are pursuing a fata morgana. We more than suspect that the final solution—if there be such—will not be in terms of a single metric . . . but of metrics."

In the previous issue of this review [300] as comprehensive a report was given about Gillott's outstanding work as space permitted. Three further installments have appeared and merit equally respectful consideration. Gillott,[295] properly, went about to check the accuracy and repeatability of measurements obtained with his space eikonometer both under normal conditions and with artificially induced size errors and found them both good—not exceeding a limit of ±0.4% even with untrained observers. He then measured a rather unselected group of 100 persons of which 17 were emmetropic within ±0.25 D.; 43, isometropic with refractive errors differing by less than 0.5 D., and the rest anisometropes. He concluded that size differences up to 0.8% are of no significance and are within normal biologic variation, making up 58% of his sample, while 42% had significant size difference. (This percentage is certainly greater than any one so far reported.) In the emmetropic group, 7 subjects showed size differences between 0.8% and 3.0%; in the isoametropic group a size difference of 0.8% to 2.0% was found in 11 cases, while in the anisoametropic group there were 16 subjects who revealed size difference greater than 1.0%. If only those subjects are counted in whom the anisoametropia was greater than 1.0 D., then 81% were found to have a larger image size difference than 1.0%. Of the seven observers who reported aniseikonia of greater than 3.0%, six belonged in this group. "In none of the observers who were examined was normal binocular vision present, without symptoms of strain."

Further analysis of Gillott's data, in another installment, reveals that not all anisoametropes have aniseikonia, just as there might be aniseikonia present in bilateral emmetropia. He finds that persons in whom the aniseikonia is in or near the vertical meridian are most likely to have visual difficulties.

Another chapter of Gillott's monograph deals with the Howard-Dolman test, its faults and merits, and the obvious relationship of the findings with this test to aniseikonia, already established by Sloan and Altman (1953). Using the improvements of the instrument offered by these authors, and adding some of his own, Gillott finally constructed a good instrument to replace the one which, by an unfortunate choice of the authorities, is as widely used as it is inaccurate. His findings prove that a Howard-Dolman type of instrument, if properly constructed, enables one to measure depth perception and aniseikonia in the horizontal meridian within an accuracy of ±0.4%.

The last part of Gillott's monograph deals with the effect of unequal retinal illumination on the frontal plane horopter. Gillott seems to have a genius for instrumentation, and he offers two further improved instruments to analyze the Helmholtz three-bar phenomenon and the so-called asymmetry effect (related to the Pulfrich phenomenon) caused by unequally illuminated retinal images. He agrees with Weale (1955) that reduced retinal illumination by reduced irradiation reduces the size of the retinal image, thus causing a kind of momentary aniseikonia. The Pulfrich effect itself, he feels, is only partially explained by this asymmetry, and some other factors must contribute to its formation. (Usually the Pulfrich effect is attributed to delayed conduction in the less-well-illuminated eye. Gillott concedes that this might be one of the factors.)

Another modification of the Howard and Dolman instrument was published by Zagora,[296] a Polish author. He retained the 6 meter distance and the rectangular "reduction" screen. However, the movable rod

can, in his apparatus, be moved not only to and fro but also laterally and up and down. It thus provides for alignment not only in depth but also in other directions. An average error of greater than 30 mm. for the lateral and depth displacement and 20 mm. for vertical placement indicate "subnormal powers of depth and height estimation." There are two fix rods, one on the left and the other on the right of the movable one. In the Howard-Dolman test the ends of the rods are concealed; in this test the lower end of the movable rod and the upper ends of the stationary rods are visible; thus certain empirical clues have obviously not been eliminated.

Cohen, Forman, and Milan [297] photographed the Ames space eikonometer target strings with a stereo camera. Artificial size differences were created by mounting size lenses before the lenses of the camera. They produced 21 slides—some with over-all size lenses of increasing magnification from 0.5% to 4.0% in 0.5% steps; others with meridional size lenses, axis at 180 degrees, in similar steps, and, finally, some with meridional size lenses, axis at 45 degrees. These slides are to be viewed in a stereo-realist viewer, and, by the subjects' reactions to the presented slides, aniseikonia can be measured. The measurements of aniseikonia in the vertical and horizontal meridian were accurate (using the data of the actual space eikonometer as standard) within 0.5%. As far as oblique aniseikonia was concerned, no definite conclusions could be drawn, though the trend of measurements seemed to be the same with both the space eikonometer and the new screening device.

Burnside and Langley [298] produced stereograms similar to the patterns used in the older type of Dartmouth eikonometers, both for the stereoscope and for the major amblyoscope. With these stereograms aniseikonia in the vertical and horizontal meridian can be, if not accurately, at least approximately measured.

Curtin [299] presented 11 patients in whom after successful retinal detachment surgery the image in the eye operated on seemed to be reduced. Scleral diathermy was used in all these cases. Only cases with better vision than 20/70 in the eye operated on could be properly tested. The absence of significant refractive changes after surgery "argues against decreased axial length of the eye as a cause of aniseikonia." Retinal edema or stretching of the reattached retina are mentioned as possible causes.

6 E. 76th St. (21).

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Correspondence

A PHYSIOLOGICAL REEVALUATION OF THE RETINOPATHY OF PREMATURITY

To the Editor:—In order to avoid as much misconception as possible, may I comment on an article appearing in the October, 1957, issue of the ARCHIVES by I. I. Eliasoph (page 495).

I had the privilege of publishing a paper on the possible correlation of carbon dioxide (or its relative lack) in the etiology of retrolental fibroplasia, three years ago. To my knowledge that was the first article on this subject, and I would like to provide the reference should any of your readers be interested:

Fortier, E. G.: The Therapeutic Possibilities of Carbon Dioxide in the Prevention of Retrolental Fibroplasia, *Am. J. Ophth.* 38:342-348 (Sept.) 1954.

Just why Dr. Eliasoph did not give even passing notice to what is probably the only previously published article encompassing his subject is conjectural; perhaps he did not know about my article, but it is easily available, appearing in an issue of the *Journal* which contained a minor symposium on retrolental fibroplasia, with articles by Patz, Reese, Zacharias, and Krause. These are required reading for one "reevaluating" retrolental fibroplasia and could have directed Dr. Eliasoph's attention to my article.

Perhaps Dr. Eliasoph simply did not like my article, but, in view of the similarities involved, he still might well have mentioned it in order to explain wherein we disagreed or what he has added. Personally, I fail to understand what improvement is accomplished by a consideration of "CO_2 and Factor X" instead of my words, "carbon dioxide and associated catabolic products." Especially since, in one place in the article, Dr. Eliasoph seems to decide that Factor X is "probably" related to carbon dioxide or the well-recognized intermediate products of carbon dioxide formation, I am unable to picture Factor X as a new concept; it seems to be a different way of saying an old thing.

Each article in a leading journal, to be valid, should constitute a real addition to our literature; I have not published further on this subject because of the feeling that I am not able to add anything new to what has been said before.

Further, Dr. Eliasoph's article "chooses" a definition of "immature infant" which is synonymous without limitation to "premature infant"; this definition serves no useful descriptive purpose, nor is it in general usage in this manner. Dr. Hess defines an immature infant as a *full-term* infant which exhibits pathology similar to one or more of the pathologic conditions that handicap the premature infant. (Hess, J. H.: Premature and Immature Infants, in Brennemann's Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1949, Vol. 1, Chap. 42, p. 2). Certainly here is the "best" definition of "immature infant" available as well as the best source possible, and I, for one, will not accept a definition in conflict with Dr. Hess' opinion on this matter.

In fact, the lead-off reference in this article is from a commercial publication of a type not generally available for consultation even in large libraries, as opposed to the M & R Pediatric Research Conference Reports, which are usually available. I checked the three largest medical libraries in Chicago, the John Crerar, the University of Illinois, and the Northwestern University Medical School, but none of them have this publication on their shelves. A reference of this caliber has little more literary force than does a personal communication, and, even if it were not conflicting in context, it is hardly suitable as a leading reference for an article in a prominent journal.

Also, Dr. Eliasoph falls into the trap of quoting an article by Eastman as "proof" of some of the chemical characteristics of fetal blood in utero. Others

have used this reference to show that the fetal blood oxygen level in utero is "low"; Dr. Eliasoph says, "The CO_2 gradient across the placenta is 1.3 to 1.0." In the immediately preceding sentence, and presumably from the same reference, he says, "In utero CO_2 levels are relatively high. . . ." I can only say, how does he know? Cold logic will tell us that we do not have any means of inserting a needle into a vein of the occupant of a normally pregnant human uterus. Surely Eastman did not accomplish this objective or anything approaching it in determining some of the quantitative chemical characteristics of blood from recently delivered full-term infants—both normal and asphyxiated or otherwise in difficulty.

In these articles (there were several on this subject: Eastman, N. J.: Foetal Blood Studies: Part I, *Bull. Johns Hopkins Hosp.* 47:221-230, 1930; Part II, 48:261-268, 1931; Part III, 50:39-50, 1932) Eastman applies the term "foetal" to practically anything, other than cord or placenta, which has recently passed through the birth canal, including full-term normal newborn infants. In one instance he made a determination on blood from a maternal vein supplying a uterus which was exposed during section for some abnormality, but I do not remember that he claimed to have made any determinations on any premature infants at all. One more-recent article by Darling, Smith, and Young (Some Properties of Human Fetal and Maternal Blood, *J. Clin. Invest.* 20:739-747, 1941) along the same line is also similarly quoted. In this article there are cited determinations on blood from two premature infants along with a larger number of full-term newborns and, if you can prove anything from two cases, the authors showed that there was not much difference in the blood oxygen or carbon dioxide levels in prematurely born infants and full-term, recently born infants. The same criticism of the indiscriminate use of the term "fetus" applies to this latter article also.

Considering the ambiguous titles and the indiscriminate, improper application of terms in their modus, results, discussions, and conclusions, these papers are, at least, among the worst articles that have ever crept into American medical literature, and yet they are widely quoted. I think they are responsible to a large extent for the disappearance of carbon dioxide-oxygen mixtures in the treatment of prematurity, but I also think it would help some if authors always read the articles they use for references.

As you may suspect, retrolental fibroplasia still occupies many of my thoughts; I have discussed my feelings with quite a few other ophthalmologists, and nearly all have advised me to run some nursery experiments. Actually, I would love to do so but I would recognize that by so doing only a mere handful of infants would come under consideration compared to the vast numbers of infants who have already, and unwittingly, been treated with carbon dioxide added to their oxygen.

During the late twenties and most of the thirties, practically all "oxygen" that was administered to premature infants was actually a mixture of oxygen with 5% or 10% carbon dioxide, although it was ordered and recorded on nursing charts as simply "oxygen." During this era, Henderson's classic observations on the physiologic basis of respiration were so universally accepted that "oxygen" for prematures usually meant oxygen-carbon dioxide without any further thought, and large amounts of this so-called oxygen were given to prematures in high and low concentrations without any apparent difficulty. In one of his articles, Eastman admits to the frequency with which carbon dioxide mixtures were in use (Asphyxia Neonatorum, *Internat. Clin.* 2:274-298, 1936); this is important because Eastman was probably the first man of medical prominence to oppose these mixtures, but the same observation can be found in many subsequent articles by other authors on each side of this controversy. References 21, 25, and 26 in my article are representative observations to this fact. Only as the swing toward pure oxygen was accomplished was retrolental fibroplasia to become a clinical problem, and only pure oxygen can adequately explain the appearance of this disease among the larger prematures as we were observing for a while.

I can only wonder about the many references I have seen stating that prematures are doing nicely under extremely restricted oxygen or without any supplemental oxygen at all, because I have observed the beneficial effects of oxygen in prematurity. These facts will not be easily established to everyone's satisfaction except by cold statistics garnered over a long period of time in a manner that will allow comparison with classic clinical achievements of the past.

I might suggest strict conformance with the rationale of Julius Hess, who placed his statistics on the basis of weight and 48-hour survival. The importance of actually weighing a premature infant when it is admitted cannot be overly emphasized, because all too often the weight is erroneously estimated or is an outside opinion accepted without question.

I have read the papers discussed above, and my criticisms are, I believe, only constructive. I definitely do not wish these criticisms to be extended to any other articles by these authors. I know that Dr. Eastman, for example, is one of the finest men ever to be in medicine, and I certainly desire my objective criticisms to be accorded just that consideration and nothing more—and then only because his early papers are persistently being misinterpreted with regard to retrolental fibroplasia.

EDWARD G. FORTIER, M.D.
1 S. Park Ave., Lombard, Ill.

To the Editor:—I wish first of all to state that I did not know of Dr. Fortier's article and was therefore unable to credit him in my paper.

Material in the medical literature is often open to varied interpretation. Hypotheses are the stimulus for research even though these hypotheses may fail to hold true. The intent of my paper is only to stimulate thought on a subject that should not be considered a closed issue.

By consideration of certain clinical information Dr. Fortier has proposed the use of carbon dioxide in the therapy or prophylaxis against retrolental fibroplasia. My own suggestions stem from physiological and biochemical principles which have found general acceptance. It is always worth while to note that like conclusions have been reached by separate pathways.

To have comment on my paper by a scholar such as Dr. Fortier is rewarding and serves to aid our progress in understanding the affliction of retrolental fibroplasia.

IRA ELIASOPH, M.D.
65 E. 96th St., New York 28

News and Comment

ANNOUNCEMENTS

Instituto Barraquer, Competition for Ophthalmological Works.—During the present year a competition is open again for scientific papers on ophthalmological subjects. Three main prizes of either 5000, 3000, or 1000 pesetas will be granted for the best papers, as well as several prizes of 500 pesetas. Address Instituto Barraquer, Laforja 88, Barcelona, Spain.

Regulations and Conditions: 1. Any medical doctor under the age of 40, Spanish or foreigner, without regard as to his being member or not of the Institute, may participate in this competition. Members of the Board of Rectors are excluded.

2. The term for admission of these papers ends on Dec. 31 of the present year.

3. The papers may be written in the author's language and must be accompanied by an extensive summary (about 500 words); the purpose of this summary is to be translated for readers of different language.

4. The papers are to be typewritten, in double spacing, using one face of the paper only. The page number should be placed in the right upper corner, and the lemma (one word indicating the subject), in the left. They may be accompanied by illustrations, tables, etc., on cardboard, with the corresponding page number and lemma as mentioned before.

5. Accompanying the work, a card with the author's full name and address has to be enclosed in a small sealed envelope identified by the lemma.

6. The qualifying jury will be formed by the Board of Rectors, assisted by the Editorial Board, its decision being without appeal. The result of the competition will be notified to the winners after Jan. 31, 1959. The prizes will be at the disposal of the winners immediately after the jury's decision is known. The rewarded works will be published in "Estudios e Informaciones Oftalmológicos." The originals on which prizes have been bestowed remain property of Institute.

7. Works to which no prizes have been granted will be destroyed after three months or returned to the author if this is requested by letter authorizing the opening of the envelope that contains his name and address.

Instituto Barraquer, Second International Course in Ophthalmology.—The Course will be held from Sept. 16 to Oct. 1, 1958, on the premises of the Institute under the direction of Professor Ignacio Barraquer.

The program comprises a cycle of surveys and several symposia on actual ophthalmological problems with film projection and various surgical sessions with presentation of interesting cases in the Barraquer Clinic.

Moreover, an interesting recreative program has been planned (excursions, Andalusia folklore, bullfight, etc.) to which participants and those who accompany them are invited.

Administrative languages will be Spanish, French, English, German, and Italian. There will be a service for simultaneous translations from and into any of them.

For inscriptions and programs write to the Secretary of the Institute, Laforja 88, Barcelona, Spain.

PROGRAM

Wednesday, Sept. 17, Inauguration of the Course, by Prof. Ignacio Barraquer.

SURVEYS

Wednesday, Sept. 17	
G. E. Jayle	The Mesopic Visual Field
J. Legrand	The Role of Tonsils in Certain Ocular Affections
H. Katzin	Instrumentation in Ophthalmic Surgery
A. Busacca	Biomicroscopy
J. Malbran	The Optic Radiation in Man
B. Carreras Matas	Corneal Dehydration
Friday, Sept. 19	
B. W. Rycroft	Surgery of Congenital Ptosis
Saturday, Sept. 20	
G. Favaloro	Optical Centers and Tracts of the Hypothalamus
J. François	The Importance of the Electro-Retinography in the Differential Diagnosis of Tapeto-Retinal Degenerations
M. Amsler	A Study of the Aqueous Humour
Tuesday, Sept. 23	
H. Ridley	Metazoan Diseases of the Eye
L. Maggiore	Thrombosis of the Retinal Veins in Haemato-Vascular Pathology
G. Cucco	Pathology of the Retinal Veins
Thursday, Sept. 25	
L. Maggiore	Colour and Chromatic Vision in Normal and Pathological Conditions
Saturday, Sept. 27	
G. Bonamour	Some Malformations of the Papilla and Their Clinical Interest
A. Bangerter	Diagnosis and Treatment of Alterations of the Lacrimal Apparatus
G. B. Bietti	Recent Advances in the Treatment of Some Ocular Conditions
Tuesday, Sept. 30	
M. Sanchez Salorio	Non-Typical Forms of Corneal Virosis
A. Piñero Carrion	Physiological Problems of Visual Acuity
R. Bartolozzi	Orbital Tumours

SYMPOSIA

Thursday, Sept. 18: Glaucoma

With the collaboration of P. A. Chandler, D. Kravitz, A. Moreu, A. Posner, A. B. Rizzuti, and B. Strampelli

Chairman: B. Boyd

The following will take part in the discussion: J. Barraquer, B. Carreras Matas, J. François, E. Malbran, A. E. Maumenee, A. Muiños, A. Salleras, M. Sanchez Salorio, A. Schlossman, J. M. Simón, R. Troutman, and D. Vail

Friday, Sept. 19: Corneal Grafting

With the collaboration of M. Amsler, J. Barraquer, J. Legrand, R. T. Paton, F. Ridley, H. Rocha, and B. W. Rycroft

Chairman: A. Salleras

The following will take part in the discussion: G. B. Bietti, J. François, G. E. Jayle, G. B. Kara, H. Katzin, J. H. King, A. E. Maumenee, E. Schreck, and B. Strampelli

Monday, Sept. 22: Surgery of the Crystalline Lens

With the collaboration of I. Barraquer, G. B. Kara, A. E. Maumenee, A. Posner, A. Salleras, and D. Vail

Chairman: R. Troutman

The following will take part in the discussion: B. Boyd, P. A. Chandler, O. Ferrer, J. François, H. Katzin, J. Malbran, G. Rarna, H. Ridley, B. W. Rycroft, M. Sanchez Salorio, E. Schreck, and D. M. Shafer

Wednesday, Sept. 24: Plastic Lenses

With the collaboration of H. Dannheim, O. Ferrer, W. S. Reese, H. Ridley, J. Scharf, E. Schreck, and B. Stampelli

Chairman: J. Barraquer

The following will take part in the discussion: G. B. Bietti, B. Boyd, A. Huber, G. B. Kara, H. Katzin, J. H. King, J. Legrand, G. Roma, A. Salleras, C. D. Shapland, and R. Troutman

Friday, Sept. 26: Retinal Detachment

With the collaboration of S. Forni, G. Meyer-Schwickerath, P. McG. Moffatt, A. Muiños, H. Pierce, and D. Shafer

Chairman: C. D. Shapland

The following will take part in the discussion: M. Amsler, H. Arruga, A. Bangerter, G. Bonamour, B. Boyd, O. Ferrer, J. Legrand, L. Maggiore, J. Malbran, B. Strampelli, and D. Vail

Monday, Sept. 29: Strabismus

With the collaboration of H. M. Burian, C. Cueppers, A. Huber, R. Hugonnier, K. Lyle, A. Muiños, A. Schlossman

Chairman: A. Huber

The following will take part in the discussion: A. Bangerter, G. B. Bietti, P. A. Chandler, E. Malbran, G. Rama, A. Salleras, and G. Sevrin

Wednesday, Oct. 1: Closing Session

American Orthoptic Council Examination.—The annual examination of orthoptic technicians by The American Orthoptic Council will be conducted in August and October, 1958.

The written examination will be nonassembled and will take place on Thursday, Aug. 21, in certain assigned cities, and will be proctored by designated ophthalmologists.

The oral and practical examinations will be on Saturday, Oct. 11, in Chicago, just preceding the meeting of the American Academy of Ophthalmology and Otolaryngology.

Application for examination will be received by the office of the Chairman of Examinations, Frank D. Costenbader, M.D., 1605 22d St., N. W., Washington 8, D. C., and must be accompanied by the examination fee of $30. Applications will not be accepted after July 1, 1958.

Harvard Basic Science Course.—The Harvard Medical School announces courses for graduates in basic sciences in ophthalmology beginning Sept. 22, 1958, and continuing through Jan. 17, 1959. The courses and instructors are as follows:

Anatomy	Russell LeG. Carpenter, Ph.D.
Biochemistry and Histochemistry	Jin H. Kinoshita, M.D.; David G. Cogan, M.D., and
Microbiology and Aseptic Technique	Henry F. Allen, M.D. associates
Neuroanatomy	David D. Donaldson, M.D.
Neuro-Ophthalmology	Richard B. Pippitt, M.D., and associates
Pathology and Histopathology	Taylor R. Smith, M.D., and associates
Physiology and Toxicology	Alfred W. Scott, M.D.; W. Morton Grant, M.D.; Endre A. Balazs, M.D., and George Wald, Ph.D.

Visual Optics and Physiology	Paul Boeder, Ph.D.

From Jan. 19 to March 11, 1959, a course in the introduction to clinical ophthalmology will be given. The subjects offered will be the following:

Refraction	Albert E. Sloane, M.D.
Ocular Motility	Abraham Pollen, M.D.
Strabismus	Virgil G. Casten, M.D.
Biomicroscopy	William P. Beetham, M.D.
Glaucoma	Robert R. Trotter, M.D.; Paul A. Chandler, M.D., and W. Morton Grant, M.D.
Retinal Detachment and Indirect Ophthalmoscopy	Charles L. Schepens, M.D.; Robert J. Brockhurst, M.D., and associates
Uveitis, Plastic Surgery, Cataract, and Miscellaneous Topics	Staff members

For further information, write to Assistant Dean, Harvard Medical School Courses for Graduates, 25 Shattuck St., Boston 15.

PERSONAL

Dr. Roderick Macdonald Jr.—The section on ophthalmology of the University of Louisville School of Medicine announces the appointment of Dr. Roderick Macdonald Jr. to the position of Assistant Professor and Executive Director of the section, effective Aug. 1, 1957. This full-time faculty appointment is a part of the expansion program in Ophthalmology, both clinical and research, which is currently under way. Dr. Macdonald was formerly Instructor in Ophthalmology at Tulane University, New Orleans.

Dr. Goodwin M. Breinin.—The department of ophthalmology of the New York University-Bellevue Medical Center has appointed Dr. Goodwin M. Breinin to the first Daniel B. Kirby professorship of research ophthalmology, it is announced by Dr. Donal Sheehan, dean.

Dr. Kirby, who was one of this country's outstanding ophthalmic surgeons, was professor of ophthalmology at New York University from 1940 to 1949 and emeritus professor until his death, in 1953. As a result of his active interest in research activities he established the Eye Surgery Fund, the purpose of which was to promote interest in ophthalmic research problems. After his death this Fund was further augmented by Mrs. Charles Melbourne Higgins, who willed a sum of money to the Fund in commemoration of her husband, Charles Melbourne Higgins.

Dr. Breinin, the first occupant of the chair, is at present director of research in the department of ophthalmology at the New York University Post-Graduate Medical School, a position which he will continue to fill. His primary field of interest has been electrophysiology of the eye, with particular reference to the extraocular muscles. His pioneering contributions have attracted widespread attention, culminating in the award of the Knapp Medal by the section of ophthalmology of the American Medical Association for original contributions in ophthalmology. There have been but eleven such recipients in the past forty-five years.

Essentially, Dr. Breinin has applied electronic engineering principles to neuromuscular problems of the eye, and so has opened new avenues of approach to the diagnosis and treatment of strabismus or crossed eyes.

It has become apparent that the techniques employed are not limited in their application solely to disturbances of the eye. A variety of generalized neuromuscular disorders, such as myasthenia gravis and muscular dystrophy, may produce diagnostic ocular electromyographic patterns. In fact, the method appears destined to be a most valuable tool with which to study the mechanisms by which the brain controls muscular activity.

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A. M. A. Archives of Ophthalmology
American Medical Association
535 North Dearborn St.
Chicago 10, Illinois

Books

A. M. A. Scientific Exhibits, 1957. Price, $15.00. Published for the American Medical Association by Grune & Stratton, Inc., 381 4th Ave., New York 16, 1958.

The publication of the 1957 exhibits remains the same as those of previous years, and, as far as ophthalmology goes, in the opinion of this reviewer, is just as useless. From every conceivable point of view the presentation of the material shown at the exhibits appears at a disadvantage in published form.

The photographs showing each individual exhibit as a whole are entirely meaningless, and the individual placards, which in the exhibits were to be read at ten to fifteen feet, are blown up so large that reading them on a printed page is even made difficult.

The Specialties in General Practice. Edited by Russell L. Cecil and Howard F. Conn. Price, $16.00. Pp. 780, with 76 illustrations, W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5, 1957.

The first edition of this book was published in 1951. The same contributors have written a short practical account of what the general practitioner should know of the specialties. The section on ophthalmology has been very ably done by Dr. R. Townley Paton, who covers this field in 33 pages. In a book of this character the value depends entirely upon the material which has been selected, and Dr. Paton has been very careful to include only those disorders which are commonly seen in the general practitioner's office. The illustrations are excellent, and the treatment is brought up to date. A book of this sort should be extremely valuable to a general practitioner if all of the sections are as well done as Dr. Paton's.

Documenta Ophthalmologica, Volume XI. Price, not given. Pp. 334. Dr. W. Junk, 13 van Stolkweg, The Hague, Netherlands, 1957.

Volume XI of *Documenta Ophthalmologica,* which is chiefly devoted to reporting advances in ophthalmology, contains an original paper by Gaffner on "angioscotometry." In a previous communication (Gaffner, F.: *Ophthalmologica* 127:293, 1954) this author described what he calls "skia scotometry." He was able to demonstrate a connection between the "skia scotomas" and the isopters as determined by perimetry, in the part of the visual field from the fovea to within approximately 30 degrees of fixation. In the present paper he establishes a mathematical relationship between the velocity of the movement of the test object and retinal summation and calculates from these data the light energy necessary for the process of summation. His conclusions are as follows: 1. A relationship may be derived for a given point of the retina involving the velocity of motion as variable and the path of summation as function, provided that all other factors are kept constant. 2. This equation in its general application is valid also for points on the retina of differing thought defined sensitivity. This condition may be expressed as an equation of the hyperbolic type $(Y-A\times[X-NB]=$a constant). 3. Based on various calculations, the attempt is made to demonstrate that for a given point on the retina the light energy necessary to reach total summation is constant and is independent of the velocity of motion of the test object as well as of the length of the path of summation. However, this principle is valid only under certain restrictions. 4. It is evident once more that in regard to stimulus response the light-adapted retina does not represent a point-for-point mosiac pattern but rather a syncytium whereat spatial effects of summation are registered over astonishingly long time intervals (seconds!).

Following this article is a report of the symposium on aqueous humor held on May 14 and 15, 1956, in Munich. Thirty-three papers are published, together with the discussions, forming a very valuable contribution to the present problems of aqueous formation and elimination.

Of particular interest are several articles on the modus operandi of acetazolamide (Diamox) in reducing intraocular pressure in man. All of the articles are either in French or in German.

Principles of Ophthalmoscopy. By John K. Erbaugh. Price, $5.50. Pp. 69. Charles C Thomas, Publisher, 301 E. Lawrence Ave., Springfield, Ill., 1957.

This book is intended to teach the principles of ophthalmoscopy to internists and neurologists. It is hard to see how it can achieve its end. In a book of only 69 pages entirely too much space has been devoted to the obvious and too little to concise descriptions and directions which the uninitiated need. It is always unfair to take paragraphs or sentences out of the context, but the beginning of Chapter 2 is an example repeated in many places: "Just as human faces differ one from the other, so do the ocular fundi. As with faces, these differences are subject to anatomic analysis, and the variations of normality separated from pathology. Through experience, an anthropologist could say, 'That is a South American Indian'; likewise an experienced ophthalmoscopist can say, 'That is a normal disc.' Yet in both cases the diagnostician has tacitly analyzed the details and compounded his impression from them. These, then, are the details, the variables, that must be considered in every examination of the disc (or optic papilla.)"

The descriptions which follow are anything but lucid, and the drawings, which the author has evidently supplied himself, leave much to be desired. The one redeeming feature of the book is a series of colored plates which have been included by courtesy of the American Optical Company, Instrument Division.

This book cannot be recommended.

Autonomic Imbalance and the Hypothalamus: Implications for Physiology, Medicine, Psychology and Neuropsychiatry. By Ernest Gellhorn. Price, $8.50. Pp. 300, with 101 figures and 13 tables. University of Minnesota Press, Minneapolis, 1957.

Between the opening quotation of the preface ("Only lunatics can be completely original") to the closing quotation of the epilogue ("It is sufficient to have attempted great things") is an experimental evaluation of the state of hypothalamic balance in animals and human subjects. Although monographs have appeared on other aspects of the autonomic nervous system, this is the first attempt in the correlation of afferent autonomic impulses with efferent autonomic activity at the level of the hypothalamus. This has imposed on the author the unavoidable difficulties of selecting the proper types of autonomic impulses (intravenous Mecholyl, arterenol, sciatic nerve stimulation, etc.), the most informative measurements of autonomic activity (heart rate, blood pressure, contraction of nicitating membrane, intestinal motility, etc.), and destructive procedures on the hypothalamus (direct injections of various drugs). The results of simultaneous application of various types of stimuli is slightly confusing, but the author generously helps the reader in the interpretation. The ophthalmologist interested in the behavior of the nictitating membrane as a prototype of the radial iris muscle would profit from the numerous experiments reported in this monograph. Figure 5 (page 16) depicts the contraction of the nictitating membrane, unaccompanied by any effect on heart rate and blood pressure, following bipolar stimulation of the posterior hypothalamus (in the cat). There are many other similar examples which indicate that the hypothalamus sends sympathetic impulses exclusively to the eye.

The War Blind in American Social Structure. By Alan G. Gowan. Price, $4.00. Pp. 237. American Foundation for the Blind, 15 W. 16th St., New York 11, 1957.

The physical and emotional adjustments required of a young and vigorous male abruptly faced with blindness are considerable. The traditions of martial glory which are taught to the youth of a nation, while admitting death and dismemberment, are usually silent about the tragedy of blindness. Yet approximately 1900 veterans of World War II are blind.

Dr. Gowman, blinded himself on the Anzio beaches by shell fire, examines the social interaction between the sighted and the blind. Socially, he makes clear, the blind are relegated to a marginal position. Some may accept the role of passive dependence expected of them, but others strive to create for themselves

an active and constructive role. The book is a study of such aggressive individuals among the blind and of the social attitudes with which they must contend. The contention is derived from neurotic anxiety which the spectacle of blindness may arouse in sighted people whose guilt feelings involve a fear of blindness and from the awkwardness of a personal relationship not clearly defined by ordinary conventions.

"Not blindness," said Helen Kellar, "but the attitude of the seeing to the blind is the hardest burden to bear."

Such a discussion illuminates an aspect of blindness little considered by society and also explains the adjustments and insights required of those who wish to be of genuine assistance to the blind. Unfortunately, the book is written for sociologists alone, and its general usefulness is limited by adherence to sociological terminology.

Lens Materials in the Prevention of Eye Injuries. By Arthur H. Keeney. Price, $3.50. Pp. 73, with 19 illustrations. Charles C Thomas, Publisher, 301 E. Lawrence Ave., Springfield, Ill., 1957.

This small monograph deals with protective lenses. The historical development of protective lens material during the last hundred years is briefly reviewed. At the present time there are on the market three main types of protective lenses, each of which is given consideration. These are as follows: (1) laminated glass lenses, (2) thermally toughened glass, and (3) plastics. The last section deals with experimental studies with protective lenses. The bulk of the material as reported in the graphs and illustrations is from Dr. Keeney's own investigative studies done at the University of Louisville, and the remainder was conducted by the U. S. Army Quartermaster Research and Development Command and the School of Aviation Medicine under Col. Victor Byrnes.

Contact Lenses. By T. W. Obrig and P. L. Salvatori. Third edition. Price, $15.00. Obrig Laboratories, Inc., 49 E. 51st St., New York 22, 1957.

This book is a curious mixture of extremely valuable data as relates to the fitting of contact glasses and their practical application and worthless claims, largely of the testimonial variety, for the use of contact glasses in various conditions. The authors, who are expert in their field and who have been pioneers in the fitting of contact lenses in this country, present in this third edition what is probably the best text in English on this subject. It is too bad that they have not been more selective in the material they have published, such as, for example, their inclusion of the recommendation of contact glasses for retinitis pigmentosa. Statments such as, "Contact lenses have proved of considerable aid in retinitis pigmentosa, not as a cure, but as a means of prolonging useful vision for periods beyond that possible without their aid," detract from a book of this character and make the whole suspect.

Included in this third edition are all of the recently developed forms of corneal lenses, a summary of the Army Medical Research Report No. 99 on contact lenses, and all of the patents in the U. S. Patent Office which have been granted for contact lenses, from the first one by J. F. Volle, on March 3, 1903, to date.

If the authors would omit the anatomical, physiological, and clinical data which can be obtained much more authoritatively and much more lucidly from other texts, and would limit their presentation to the practical side of contact lens fitting, the book could undoubtedly be recommended as *the* authoritative volume on contact lenses.

Individual Differences in Night Vision Efficiency. By M. H. Pirenne, F. H. C. Marriott and E. F. O'Doherty. Price, $1.52. Pp. 83. Her Majesty's Stationery Office, P. O. Box 569, London, S. E. 1 (American Agent—British Information Services, 45 Rockefeller Plaza, New York 20), 1957.

This volume is the result of a follow-up examination of personnel in the military service in England during the last war, who had previously had their

dark adaptation recorded. For those interested in the physiology of dark adaptation, this book will be of special interest, containing as it does material which was previously restricted because of the war.

The Vertebrate Visual System. By Stephen Polyak, M.D. (edited by Heinrich Kluver). Price, $45.00. Pp. 1408, including index and bibliography, with 551 illustrations (27 in color). The University of Chicago Press, 5750 Ellis Ave., Chicago 37, 1957.

In 1941 Stephen Polyak published "The Retina," a book which won him world-wide acclaim. This masterpiece embodies his own researches on the histology of the primate retina. Since its publication this has been the standard source of reference for those interested in retinal morphology. Polyak's interests were far wider than the histological organization of the retina, however, and in that book one can find considerable speculation on how the retina functions, based on retinal morphology. Many of his ideas have been accepted by his contemporaries who have studied retinal function by chemical or electrophysiological techniques, and Granit has paid respect and gratitude to Polyak for his histological contributions and functional interpretations. According to Kluver, his intimate friend and confidant, it was Polyak's purpose to round up his life's work by publishing a compendium of existing knowledge of the anatomy and physiology of the rest of the visual system which would be a fit companion to "The Retina."

"The Vertebrate Visual System" resulted. Before he had time to finish the manuscript, however, death overtook him, on March 9, 1955. Had it not been for Kluver, this second great contribution to our knowledge of the function of the eye would have been lost. Kluver decided that if Polyak's illness, which threatened him with sudden death or blindness during his last months, should prevent him from finishing the manuscript, then he, Kluver, would make it his responsibility to finish it. The knowledge of this undoubtedly must have given Polyak great comfort and strength in his last illness, during which he worked almost beyond human endurance to get the job done. True to his promise, Kluver did for his friend what is probably the most arduous and most distasteful part of writing any book, namely, reading proof, matching illustrations with legends, preparing the index, checking the index, checking the bibliography, and the thousand and one details which require meticulous care and enormous blocks of time and seem so unrewarding. In the last analysis, however, these are just as important as writing the book. The usefulness of many otherwise splendid contributions has been seriously curtailed by lack of attention to these details. It is not too much to say Kluver should really be considered a co-author of this volume. His name would lend luster to any book concerned with visual processes, as he is one of the recognized outstanding contributors in this field. It is an earnest of Kluver's greatness that he only permitted himself to be connected with this publication as the editor.

The book is divided into four parts: historical, anatomical, pathological, and biological. Polyak was always interested in the origin of concepts of visual function and with the men who developed these ideas. His own researches were largely stimulated by these sources. It is not surprising, therefore, that a large portion of this book should be devoted to the historical aspect of the subject and that a rather larger number of illustrations than usual are pictures of past and present men who have influenced thinking in vision. The bibliography contains approximately 10,000 references, and is almost complete in the field of anatomy of the visual organs.

The anatomical portion is a review of the material in "The Retina" and includes the higher visual centers of the vertebrate visual system. The third section deals with the pathoanatomical basis of disturbed vision, with emphasis on the localization of field defects. All ophthalmologists and neurologists will find this section of great interest.

The last section deals with the origin and development of the vertebrate eye and how vision has aided the evolutionary development of the primates. In his preface Polyak states, " 'The Vertebrate Visual System' " represents the almost continuous labor of nearly three decades. It was a great, and for the most part a pleasant, privilege to write it. Its success will be measured by its service as a source of instruction to all those in any way interested in vision, and by the encouragement it may give to further research." There is little question that Polyak's hopes for the book will be realized and that for years to come it will enrich our literature.

While the price of this book may seem an obstacle to its purchase, no library can afford to be without a copy of it.

Therapeutique médicale oculaire: Tome I. Edited by J. Sédan, G. W. Jayle, J. Malbran, J. François, and G. Calamandrei. Price, fr. 6000. Pp. 1646 (2 vols.), with 2 color plates and numerous illustrations. Masson et Cie, 120 Blvd. St. Germain, Paris 6e, France, 1957.

A large and impressive list of well-known ophthalmologists over the world have contributed to this volume on medical therapeutics in ophthalmology, published in French. In America the following ophthalmologists have contributed: Drs. Walter S. Atkinson, John G. Bellows, Hermann M. Burian, Virgil G. Casten, Ramon Castroviejo, Derrick Vail, Herman Elwyn, Michael J. Hogan, Robert Hollenhorst, Irving H. Leopold, Charles L. Schepens, David Shoch, Saul Sugar, Frederick H. Theodore, and Phillips Thygeson. It is a monumental work. The first volume contains an analytical nomenclature of drugs and their pharmacodynamics. There is also a section on physical agents such as radiotherapy, β-radiation, radioisotopes, ionophoresis, light therapy, ultrasonic therapy, freezing, aerosols, and mechanotherapy, and there is even a chapter on the effects of climate. The rest of the volume is concerned with the therapeutics of the eye and its adnexa, the first volume treating the external eye and the second volume, the retina, choroid, optic nerve, lens, glaucoma, vitreous, and refraction. The work ends with a section on the therapeutics of general diseases which have ocular manifestations and a section on ocular hygiene.

This book is undoubtedly of great value, and it is to be hoped that it will have an English translation so that it will be made available to those who do not read French fluently.

The Glaucomas. By H. Saul Sugar, M.D. Second edition. Price, $13.50. Pp. 516, with 164 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33d St., New York 16, 1957.

The voluminous literature on the subject of glaucoma during the past few years has made imperative an extensive revision of this basic textbook. The work has been expanded to include new chapters on tonography and on goniotomy and goniopuncture. The chapters on aqueous humor, acute glaucoma, anatomy, and the use of drugs have been extensively revised to keep pace with recent developments in these areas.

The author's attempt to include all recent contributions while maintaining brevity and simplicity have resulted in a less readable text, which lacks the authoritative ring of the author's personal convictions. Although the book will be a useful reference work, its broad scope and lack of clear definition, especially in the chapters on primary glaucoma, will make it less useful as a basic text for students and practitioners.

Methods in Medical Research: Vol. 7. Edited by James V. Warren. Price, $7.50. Pp. 237, including index, with numerous charts and tables. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.

The seventh volume of this annual series contains a section on methods of study of the histology and cytology of the retina by E. N. Willner. Thus, for the first time ophthalmology is represented in this valuable technical handbook. For all those interested in the preparation of microscopic sections of the retina, this volume will be of value. The section contains 117 references.

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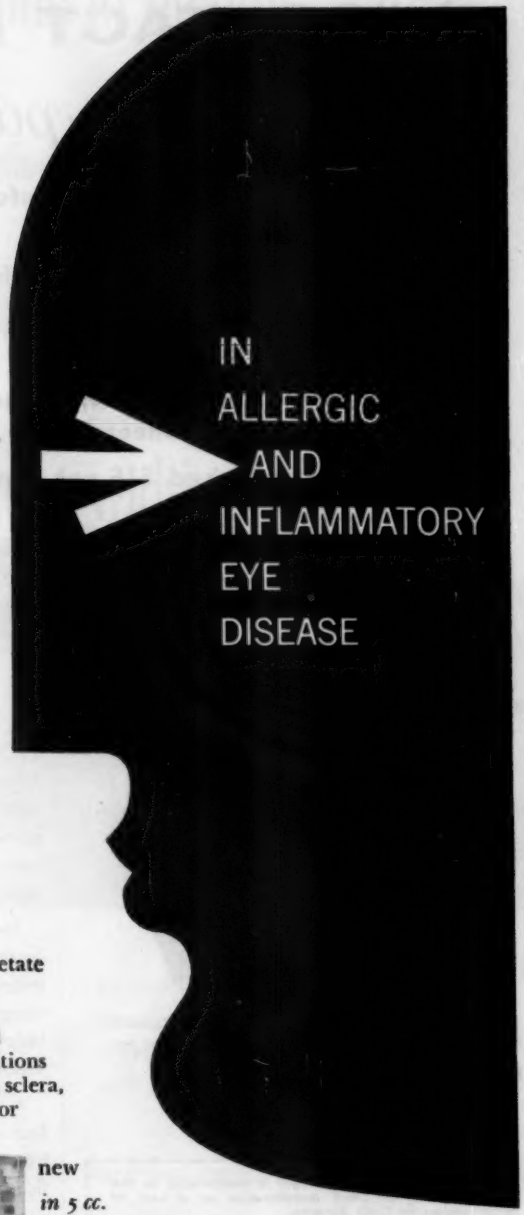

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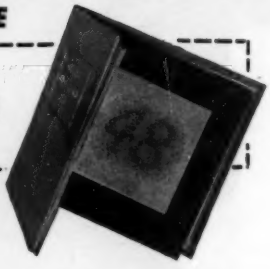

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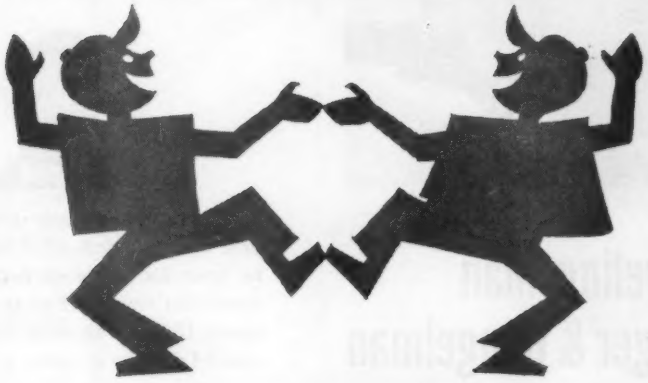

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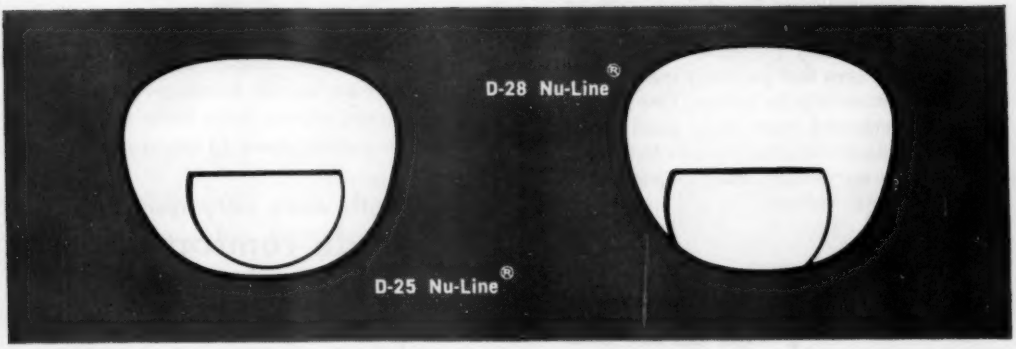

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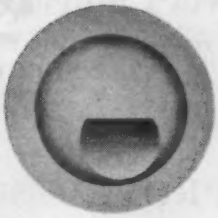

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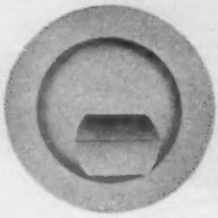

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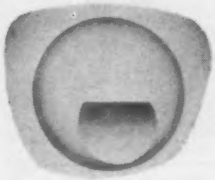

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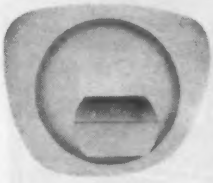

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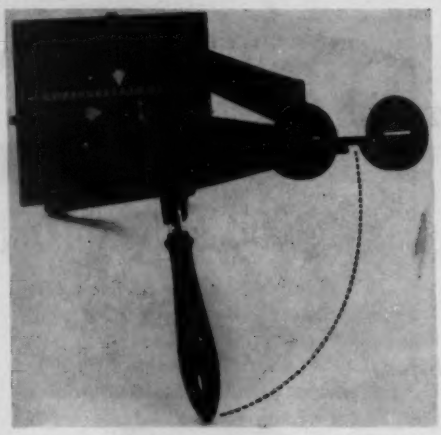

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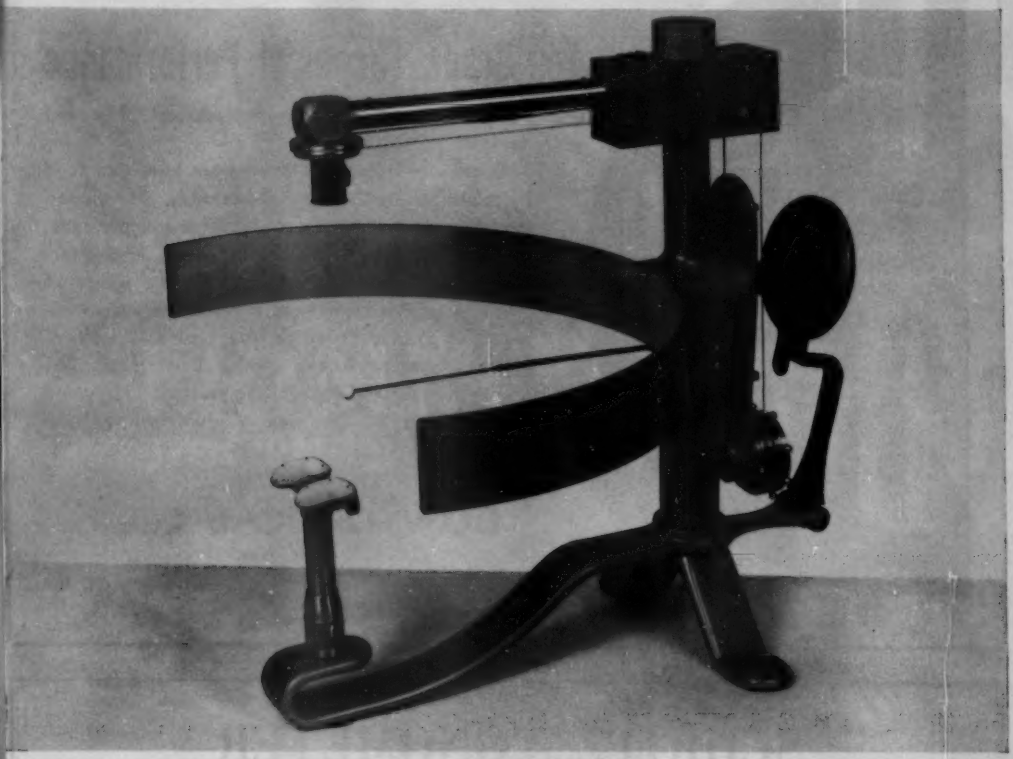

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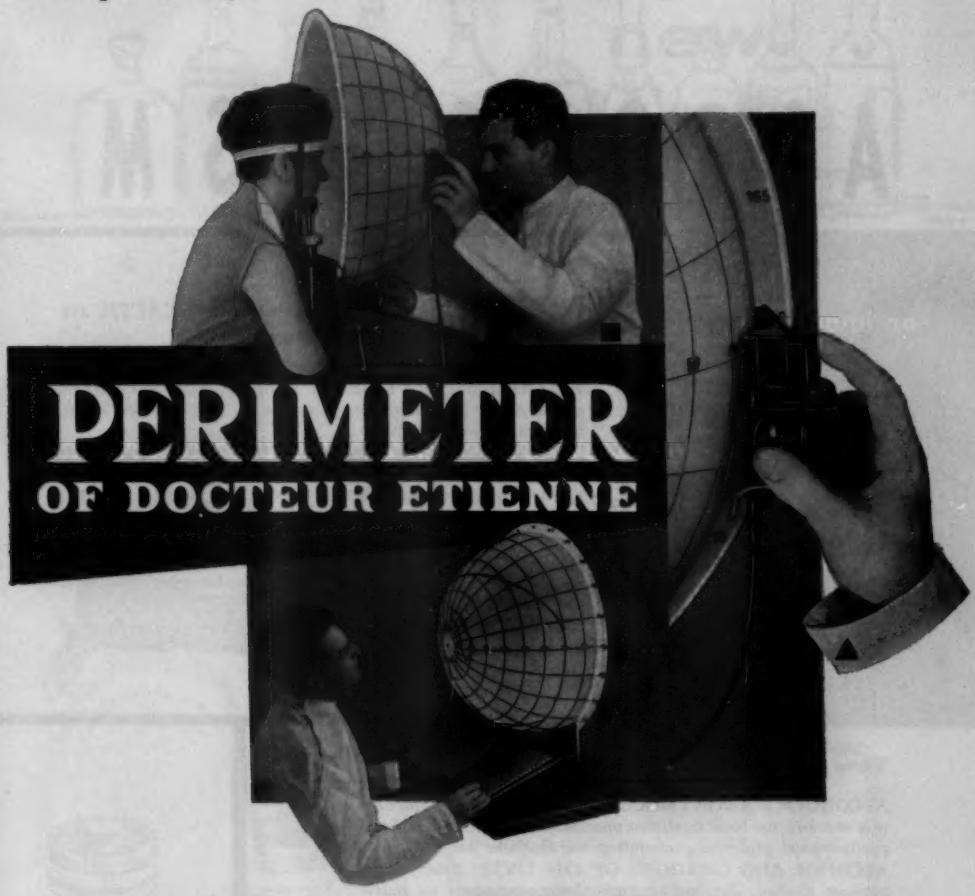

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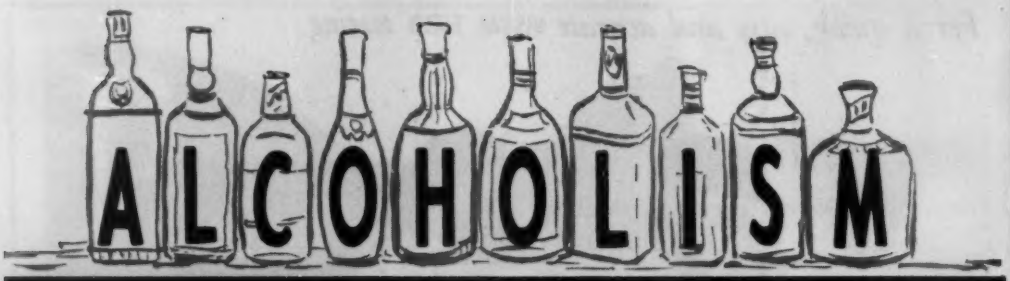

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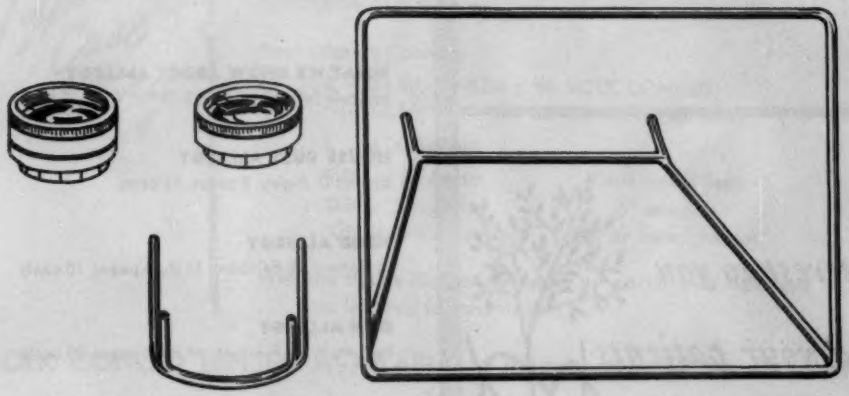

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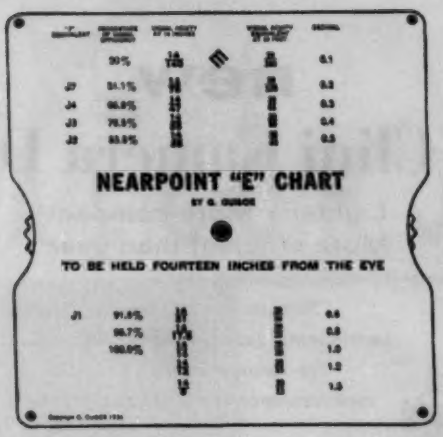

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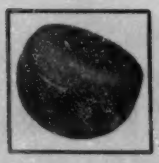
THE  BRAWNER G-L

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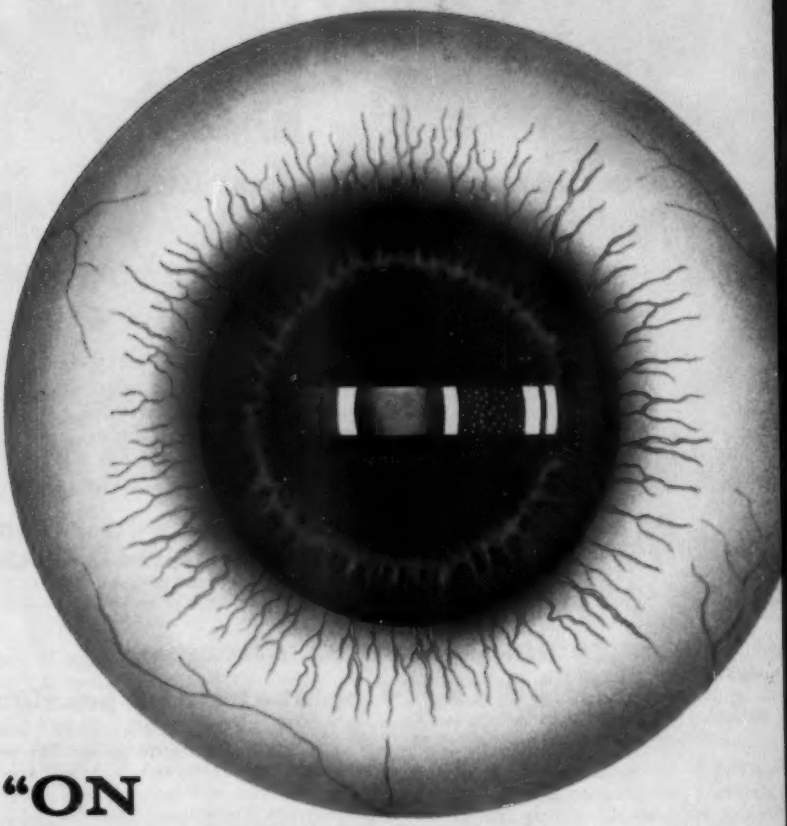

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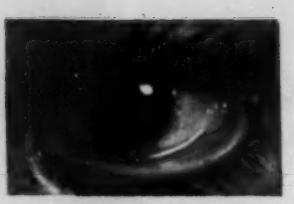

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1. Schlegel, H. E., Jr., and Swan, K. C.: A.M.A. Arch. Ophth. *51*:663 (May) 1954.
2. Emmerich, R.; Carter, G. Z., and Berens, C.: Am. J. Ophth. *40*:841 (Dec.) 1955.

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